

Tran 09/738,954

=> d his

(FILE 'HOME' ENTERED AT 10:45:57 ON 18 MAR 2002)

FILE 'MEDLINE, BIOSIS, HCAPLUS, WPIDS' ENTERED AT 10:46:08 ON 18 MAR 2002

E CRAVATT B/AU
L1 143 S E3-7
E SORENSEN E/AU
L2 581 S E3-E25
L3 93 S E44-52
E PATRICELLI M/AU
L4 49 S E3-7
E LOVATO M/AU
L5 48 S E3-8 OR E10-11
E ADAM G/AU
L6 1479 S E3-20
E ADAM GREGORY/AU
L7 8 S E3-4
E ADAM GREG/AU
L8 20 S E3-4
L9 2342 S L1-L8
L10 5145 S PROTEOM?
L11 21 S L9 AND L10
E WO2001077668/PN
L12 2 S E3
L13 609566 S SCREEN?
L14 400898 S PROBE#
L15 41572 S BIOACTIV? OR BIO ACTIV?
L16 22 S L14 AND L6
L17 12 S L16 AND (TARGET? OR L15 OR ENZYM? OR PROTEIN#)
L18 30 S L11 OR L17
L19 17 DUP REM L18 (13 DUPLICATES REMOVED)
L20 40 S L11 OR L16
L21 25 DUP REM L20 (15 DUPLICATES REMOVED)

17. A method for determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins in each of said proteomic mixtures, said related proteins related in having a common functionality for conjugation at an active site, said method comprising:

- (1) combining each of said proteomic mixtures in wild-type form with a probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;
- (2) determining the presence of target members conjugated with said probe in said proteomic mixtures;
- (3) analyzing for the presence of target members conjugated with said probe using simultaneous individual capillary electrokinetic analysis or capillary HPLC;

whereby when said target members are conjugated to target members in said proteomic mixtures, the presence of active target members is determined.

19. A method for determining in a proteomic mixture the presence of active target members of a group of related enzymes, said related enzymes related in having a common functionality for conjugation at an active site, said method comprising:

- (1) combining said proteomic mixture in wild-type form with a probe comprising a reactive functionality specific for said active site when active, under conditions for conjugation of said probe to said target members;
- (2) combining said proteomic mixture after non-specific deactivation with said probe under said same conditions;
- (3) determining the presence of target members conjugated with said probe in said proteomic mixtures in active and inactive form;

whereby when said probe is conjugated to at least one target member in said proteomic mixture in active form and in lesser amount in inactive form, the presence of active members is determined.

=> fil medline biosis hcaplus wpids
FILE 'MEDLINE' ENTERED AT 10:56:43 ON 18 MAR 2002

FILE 'BIOSIS' ENTERED AT 10:56:43 ON 18 MAR 2002
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FILE 'WPIDS' ENTERED AT 10:56:43 ON 18 MAR 2002
COPYRIGHT (C) 2002 DERWENT INFORMATION LTD

=> d que 19;d his 110-

L1 143 SEA ("CRAVATT B"/AU OR "CRAVATT B F"/AU OR "CRAVATT BEN"/AU OR "CRAVATT BEN F"/AU OR "CRAVATT BENJAMIN F"/AU)

L2 581 SEA ("SORENSEN E"/AU OR "SORENSEN E A"/AU OR "SORENSEN E B"/AU OR "SORENSEN E C"/AU OR "SORENSEN E D"/AU OR "SORENSEN E E"/AU OR "SORENSEN E F"/AU OR "SORENSEN E H"/AU OR "SORENSEN E I"/AU OR "SORENSEN E J"/AU OR "SORENSEN E K"/AU OR "SORENSEN E L"/AU OR "SORENSEN E M"/AU OR "SORENSEN E M B"/AU OR "SORENSEN E N"/AU OR "SORENSEN E P"/AU OR "SORENSEN E P V"/AU OR "SORENSEN E R"/AU OR "SORENSEN E S"/AU OR "SORENSEN E T"/AU OR "SORENSEN E TODD"/AU OR "SORENSEN E V"/AU OR "SORENSEN E W"/AU)

L3 93 SEA ("SORENSEN ERIK"/AU OR "SORENSEN ERIK D"/AU OR "SORENSEN ERIK J"/AU OR "SORENSEN ERIK JOSEPH"/AU OR "SORENSEN ERIK LAHN"/AU OR "SORENSEN ERIK N"/AU OR "SORENSEN ERIK NIEL"/AU OR "SORENSEN ERIK S"/AU OR "SORENSEN ERIK SCHWARTZ"/AU)

L4 49 SEA ("PATRICELLI M"/AU OR "PATRICELLI M P"/AU OR "PATRICELLI MATTHEW"/AU OR "PATRICELLI MATTHEW P"/AU OR "PATRICELLI MATTHEW PETER"/AU)

L5 48 SEA ("LOVATO M"/AU OR "LOVATO M A"/AU OR "LOVATO M B"/AU OR "LOVATO M L"/AU OR "LOVATO M P"/AU OR "LOVATO M V"/AU) OR ("LOVATO MARTHA"/AU OR "LOVATO MARTHA A"/AU)

L6 1479 SEA ("ADAM G"/AU OR "ADAM G A"/AU OR "ADAM G B"/AU OR "ADAM G C"/AU OR "ADAM G D"/AU OR "ADAM G E"/AU OR "ADAM G F"/AU OR "ADAM G G"/AU OR "ADAM G H"/AU OR "ADAM G H M"/AU OR "ADAM G I"/AU OR "ADAM G I R"/AU OR "ADAM G K"/AU OR "ADAM G M"/AU OR "ADAM G P"/AU OR "ADAM G S"/AU OR "ADAM G V"/AU OR "ADAM G W"/AU)

L7 8 SEA ("ADAM GREGORY"/AU OR "ADAM GREGORY C"/AU)

L8 20 SEA ("ADAM GREG"/AU OR "ADAM GREG C"/AU)

L9 2342 SEA (L1 OR L2 OR L3 OR L4 OR L5 OR L6 OR L7 OR L8)

(FILE 'MEDLINE, BIOSIS, HCAPLUS, WPIDS' ENTERED AT 10:46:08 ON 18 MAR 2002)

L10 5145 S PROTEOM?
L11 21 S L9 AND L10
E WO2001077668/PN
L12 2 S E3
L13 609566 S SCREEN?
L14 400898 S PROBE#
L15 41572 S BIOACTIV? OR BIO ACTIV?
L16 22 S L14 AND L6
L17 12 S L16 AND (TARGET? OR L15 OR ENZYM? OR PROTEIN#)

Tran 09/738,954

L18 30 S L11 OR L17
L19 17 DUP REM L18 (13 DUPLICATES REMOVED)
L20 40 S L11 OR L16
L21 25 DUP REM L20 (15 DUPLICATES REMOVED)

FILE 'MEDLINE, BIOSIS, HCAPLUS, WPIDS' ENTERED AT 10:56:43 ON 18 MAR 2002

=> d bib ab 1-25

L21 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 1
AN 2001:763323 HCAPLUS

DN 135:315598

TI Methods for proteomic analysis using activity based probes for target proteins

IN Cravatt, Benjamin F.; Sorensen, Erik; Patricelli, Matthew; Lovato, Martha; Adam, Gregory

PA Scripps Research Institute, USA

SO PCT Int. Appl., 119 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077684	A2	20011018	WO 2000-US34187	20001215
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 2000-195954 P 20000410

US 2000-212891 P 20000620

US 2000-222532 P 20000802

OS MARPAT 135:315598

AB The present invention provides methods for analyzing proteomes, as cells or lysates. The anal. is based on the use of probes that have specificity to the active form of proteins, particularly enzymes and receptors. The probes can be identified in different ways. In accordance with the present invention, a method is provided for generating and screening compd. libraries that are used for the identification of lead mols., and for the parallel identification of their biol. targets. By appending specific functionalities and/or groups to one or more binding moieties, the reactive functionalities gain binding affinity and specificity for particular proteins and classes of proteins. Such libraries of candidate compds., referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biol. activities or target proteins.

L21 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2002 ACS DUPLICATE 2

AN 2001:763309 HCAPLUS

DN 135:315597

TI Methods for bioactivity screening of candidate compounds using activity based probes

IN Cravatt, Benjamin F.; Sorensen, Erik; Patricelli, Matthew; Lovato, Martha; Adam, Gregory

PA Scripps Research Institute, USA

SO PCT Int. Appl., 118 pp.

CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001077668	A2	20011018	WO 2000-US34167	20001215
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRAI	US 2000-195954	P	20000410		
	US 2000-212891	P	20000620		
	US 2000-222532	P	20000802		
OS	MARPAT 135:315597				
AB	The present invention provides methods for analyzing proteomes, as cells or lysates. The anal. is based on the use of probes that have specificity to the active form of proteins, particularly enzymes and receptors. The probes can be identified in different ways. In accordance with the present invention, a method is provided for generating and screening compd. libraries that are used for the identification of lead mols., and for the parallel identification of their biol. targets. By appending specific functionalities and/or groups to one or more binding moieties, the reactive functionalities gain binding affinity and specificity for particular proteins and classes of proteins. Such libraries of candidate compds., referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biol. activities or target proteins.				
L21	ANSWER 3 OF 25	MEDLINE		DUPPLICATE 3	
AN	2001354896	MEDLINE			
DN	21197760	PubMed ID: 11300781			
TI	Profiling serine hydrolase activities in complex proteomes .				
AU	Kidd D; Liu Y; Cravatt B F				
CS	The Skaggs Institute for Chemical Biology and Department of Cell Biology, The Scripps Research Institute, La Jolla, California 92037, USA.				
NC	CA87660 (NCI)				
SO	BIOCHEMISTRY, (2001 Apr 3) 40 (13) 4005-15. Journal code: A0G; 0370623. ISSN: 0006-2960.				
CY	United States				
DT	Journal; Article; (JOURNAL ARTICLE)				
LA	English				
FS	Priority Journals				
EM	200106				
ED	Entered STN: 20010625 Last Updated on STN: 20010625 Entered Medline: 20010621				
AB	Serine hydrolases represent one of the largest and most diverse families of enzymes in higher eukaryotes, comprising numerous proteases, lipases, esterases, and amidases. The activities of many serine hydrolases are tightly regulated by posttranslational mechanisms, limiting the suitability of standard genomics and proteomics methods for the functional characterization of these enzymes. To facilitate the global analysis of serine hydrolase activities in complex proteomes , a biotinylated fluorophosphonate (FP-biotin) was recently synthesized and shown to serve as an activity-based probe for several members of this				

enzyme family. However, the extent to which FP-biotin reacts with the complete repertoire of active serine hydrolases present in a given **proteome** remains largely unexplored. Herein, we describe the synthesis and utility of a variant of FP-biotin in which the agent's hydrophobic alkyl chain linker was replaced by a more hydrophilic poly(ethylene glycol) moiety (FP-peg-biotin). When incubated with both soluble and membrane **proteomes** for extended reaction times, FP-biotin and FP-peg-biotin generated similar "maximal coverage" serine hydrolase activity profiles. However, kinetic analyses revealed that several serine hydrolases reacted at different rates with each FP agent. These rate differences were exploited in studies that used the biotinylated FPs to examine the target selectivity of reversible serine hydrolase inhibitors directly in complex **proteomes**. Finally, a general method for the avidin-based affinity isolation of FP-biotinylated proteins was developed, permitting the rapid and simultaneous identification of multiple serine peptidases, lipases, and esterases. Collectively, these studies demonstrate that chemical probes such as the biotinylated FPs can greatly accelerate both the functional characterization and molecular identification of active enzymes in complex **proteomes**.

L21 ANSWER 4 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
4
AN 2001:561475 BIOSIS
DN PREV200100561475
TI Direct visualization of serine hydrolase activities in complex **proteomes** using fluorescent active site-directed probes.
AU Patricelli, Matthew P. (1); Giang, Dan K.; Stamp, Lisa M.;
Burbaum, Jonathan J.
CS (1) ActivX Biosciences, 11025 N Torrey Pines Road, Suite 120, La Jolla,
CA, 92037; mattp@activx.com USA
SO Proteomics, (September, 2001) Vol. 1, No. 9, pp. 1067-1071. print.
ISSN: 1615-9853.
DT Article
LA English
SL English
AB The field of biochemistry is currently faced with the enormous challenge of assigning functional significance to more than thirty thousand predicted protein products encoded by the human genome. In order to accomplish this daunting task, methods will be required that facilitate the global analysis of proteins in complex biological systems. Recently, methods have been described for simultaneously monitoring the activity of multiple enzymes in crude **proteomes** based on their reactivity with tagged chemical probes. These activity based probes (ABPs) have used either radiochemical or biotin/avidin-based detection methods to allow consolidated visualization of numerous enzyme activities. Here we report the synthesis and evaluation of fluorescent activity based probes for the serine hydrolase super-family of enzymes. The fluorescent methods detailed herein provide superior throughput, sensitivity, and quantitative accuracy when compared to previously described ABPs, and provide a straight-forward platform for high-throughput **proteome** analysis.

L21 ANSWER 5 OF 25 MEDLINE
AN 2001339073 MEDLINE
DN 21133860 PubMed ID: 11237963
TI Experimental MR imaging-guided interstitial cryotherapy of the brain.
AU Tacke J; Speetzen R; Adam G; Sellhaus B; Glowinski A; Heschel I;
Schaffter T; Schorn R; Grosskortenhaus S; Rau G; Gunther R W
CS Department of Diagnostic Radiology, University of Technology, Aachen,
Germany.

SO AJNR. AMERICAN JOURNAL OF NEURORADIOLOGY, (2001 Mar) 22 (3) 431-40.
 Journal code: 3AG; 8003708. ISSN: 0195-6108.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200106
 ED Entered STN: 20010618
 Last Updated on STN: 20010618
 Entered Medline: 20010614
 AB BACKGROUND AND PURPOSE: Hyperthermal ablation techniques such as laser or RF ablation require dedicated heat-sensitive MR imaging sequences for monitoring MR imaging--guided interventions. Because cryotherapy does not have these limitations, the purpose of this study was to evaluate the feasibility of MR imaging--guided percutaneous cryotherapy of the brain. METHODS: An experimental cryoprobe with an outer diameter of 2.7 mm was inserted into the right frontal lobe of 11 healthy pigs under MR imaging control. Freezing procedures were monitored by using an interventional 1.5-T magnet and a gradient-echo sequence with radial k-space trajectories, a fast T2-weighted single-shot spin-echo sequence, and a T1-weighted single-shot gradient-echo sequence. In three animals, the procedure was also monitored by using dynamic CT. A freeze-thaw cycle with a duration of 3 minutes was repeated three times per animal. Follow-up MR images were obtained 3, 7, and 14 days after cryotherapy by using conventional MR sequences. Six animals were killed 7 days after intervention, and five animals were killed 14 days after intervention. The brains were sectioned, and the histologic findings of the lesions were compared with the MR imaging appearance. RESULTS: No artifacts due to the probe were observed on the MR images or CT scans. The ice formation (mean diameter, 12.5 mm) was very well delineated as a signal-free sphere. MR monitoring of the freezing procedure yielded a significantly higher ice:tissue contrast than did CT. The size of the ice ball as imaged by MR imaging and CT during the intervention correlated well with the MR imaging appearance of the lesions at the 14-day follow-up examination and with the histologic findings. Histologically, coagulation necrosis and gliosis were found, surrounded by a transition zone of edema and a disrupted blood-brain barrier, corresponding to a contrast-enhancing rim around the lesions on follow-up MR images. CONCLUSION: MR imaging-guided cryotherapy of the brain is possible and allows a precise prediction of the resulting necrosis. MR imaging of the freezing process does not require heat-sensitive sequences and is superior to CT for monitoring of cryoablation.

L21 ANSWER 6 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
 5
 AN 2001:514429 BIOSIS
 DN PREV200100514429
 TI Mapping active site space and reactivity in complex **proteomes**.
 AU Cravatt, Benjamin F. (1); Adam, Gregory C.;
 Sorensen, Erik J.
 CS (1) Departments of Cell Biology and Chemistry, Skaggs Institute for
 Chemical Biology, Scripps Research Institute, 10550 N. Torrey Pines Rd.,
 La Jolla, CA, 92037: cravatt@scripps.edu USA
 SO Abstracts of Papers American Chemical Society, (2001) Vol. 222, No. 1-2,
 pp. BIOL137. print.
 Meeting Info.: 222nd National Meeting of the American Chemical Society
 Chicago, Illinois, USA August 26-30, 2001 American Chemical Society
 . ISSN: 0065-7727.
 DT Conference
 LA English

- SL English
- AB The field of **proteomics** aims to characterize dynamics in protein function on a global scale. However, several classes of enzyme are subject to posttranslational forms of active site-directed regulation, limiting the utility of conventional **proteomics** techniques for the characterization of these proteins. Recently, we have initiated a research program aimed at generating chemical probes that interrogate the status of enzyme active sites in crude **proteomes**, thereby facilitating the functional characterization of enzymes in samples of high complexity. We will describe our efforts to map active site space and structure for several enzyme classes that collectively segregate into two general categories: 1) enzymes for which **proteomics**-compatible, active site-directed affinity agents are well-defined, and 2) enzymes for which **proteomics**-compatible, active site-directed affinity agents are currently lacking.
- L21 ANSWER 7 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 6
- AN 2001:492117 BIOSIS
- DN PREV200100492117
- TI Redirecting the specific reactivity of a natural product and its application to functional **proteomics**.
- AU Tamiya, Junko (1); Cravatt, Benjamin F.; Sorensen, Erik J.
(1)
- CS (1) Department of Chemistry, Skaggs Institute for Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA, 92037: jtamiya@scripps.edu USA
- SO Abstracts of Papers American Chemical Society, (2001) Vol. 222, No. 1-2, pp. BIOL90. print.
Meeting Info.: 222nd National Meeting of the American Chemical Society Chicago, Illinois, USA August 26-30, 2001 American Chemical Society . ISSN: 0065-7727.
- DT Conference
- LA English
- SL English
- AB Activity-based protein profiling aims to create chemical agents to profile changes in enzyme activity in complex **proteomes**. Combining this methodology with a natural product scaffold, a library of biotinylated analogs of the natural product fumagillin was constructed and tested against complex **proteomes**. Fumagillin is an angiogenesis inhibitor, which contains an electrophilic spiroexpoxide and a hydrophobic side chain. The spiroepoxide covalently modifies the metalloprotease methionine aminopeptidase-2 (MetAp-2). Variation of the side chain to both hydrophobic and hydrophilic moieties redirected this natural product, facilitating the specific labeling of a diverse number of proteins directly in complex **proteomes**.
- L21 ANSWER 8 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 7
- AN 2001:491354 BIOSIS
- DN PREV200100491354
- TI Profiling the specific reactivity of the **proteome** with non-directed chemical libraries.
- AU Adam, Gregory C. (1); Cravatt, Benjamin F.; Sorensen, Erik J.
- CS (1) Department of Chemistry, Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA, 92037: gadam@scripps.edu USA
- SO Abstracts of Papers American Chemical Society, (2001) Vol. 222, No. 1-2, pp. BIOL84. print.
Meeting Info.: 222nd National Meeting of the American Chemical Society

Chicago, Illinois, USA August 26-30, 2001 American Chemical Society
 . ISSN: 0065-7727.

DT Conference
 LA English
 SL English
 AB Through screening the **proteome** with chemical probes bearing functionalities common to organic synthesis but underutilized in biology, proteins or classes of proteins susceptible to new forms of inactivation may be discovered. A library of biotinylated sulfonates was synthesized and its members applied to complex **proteomes** under conditions that distinguish patterns of specific protein reactivity. Individual sulfonates exhibited unique profiles of **proteome** reactivity that in extreme cases appeared completely orthogonal to one another. Targets of the tagged sulfonate library include members of multiple structurally and mechanistically distinct enzyme families. Progress towards understanding the mechanisms by which the sulfonate probes react with their discrete enzyme targets will be reported. These data reveal that a non-directed approach towards probing the chemical reactivity of the **proteome** can readily identify compounds possessing selective and unanticipated biological activities.

L21 ANSWER 9 OF 25 MEDLINE DUPLICATE 8
 AN 2001269063 MEDLINE
 DN 21110454 PubMed ID: 11182321
 TI Profiling the specific reactivity of the **proteome** with non-directed activity-based **probes**.
 AU Adam G C; Cravatt B F; Sorensen E J
 CS The Skaggs Institute for Chemical Biology, La Jolla, CA 92037, USA.
 NC CA87660 (NCI)
 SO CHEMISTRY AND BIOLOGY, (2001 Jan) 8 (1) 81-95.
 Journal code: CNA; 9500160. ISSN: 1074-5521.
 CY England: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200105
 ED Entered STN: 20010529
 Last Updated on STN: 20010529
 Entered Medline: 20010521
 AB BACKGROUND: The field of **proteomics** aims to characterize dynamics in protein function on a global level. However, several classes of proteins, in particular low abundance proteins, remain difficult to characterize using standard **proteomics** technologies. Recently, chemical strategies have emerged that profile classes of proteins based on activity rather than quantity, thereby greatly facilitating the analysis of low abundance constituents of the **proteome**. RESULTS: In order to expand the classes of proteins susceptible to analysis by activity-based methods, we have synthesized a library of biotinylated sulfonate esters and applied its members to complex **proteomes** under conditions that distinguish patterns of specific protein reactivity. Individual sulfonates exhibited unique profiles of **proteome** reactivity that in extreme cases appeared nearly orthogonal to one another. A robustly labeled protein was identified as a class I aldehyde dehydrogenase and shown to be irreversibly inhibited by members of the sulfonate library. CONCLUSIONS: Through screening the **proteome** with a non-directed library of chemical **probes**, diverse patterns of protein reactivity were uncovered. These **probes** labeled protein targets based on properties other than abundance, circumventing one of the major challenges facing contemporary **proteomics** research. Considering further that the **probes** were found to

inhibit a target enzyme's catalytic activity, the methods described herein should facilitate the identification of compounds possessing both selective **proteome** reactivities and novel bioactivities.

L21 ANSWER 10 OF 25 MEDLINE
 AN 2001177605 MEDLINE
 DN 21096038 PubMed ID: 11169803
 TI MR-guided percutaneous cryotherapy of the liver: in vivo evaluation with histologic correlation in an animal model.
 AU Tacke J; Adam G; Haage P; Sellhaus B; Grosskortenhaus S; Gunther R W
 CS Department of Diagnostic Radiology, University of Technology, Pauwelsstrasse 30, 52074 Aachen, Germany.. tacke@rad.rwth-aachen.de
 SO JOURNAL OF MAGNETIC RESONANCE IMAGING, (2001 Jan) 13 (1) 50-6.
 Journal code: BEO; 9105850. ISSN: 1053-1807.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200104
 ED Entered STN: 20010502
 Last Updated on STN: 20010502
 Entered Medline: 20010426
 AB The purpose of this study was to evaluate the feasibility of MR-guided percutaneous cryotherapy of the porcine liver and to correlate the resulting tissue necrosis with MR imaging and histology. Using an MR-compatible, argon-based cryotherapy system (CryoHit; Galil Medical Ltd., Israel) with 2- and 3-mm diameter tapered cryotherapy **probes**, MR-guided percutaneous cryotherapy was performed in seven pigs (mean body weight, 40 kg) under general anesthesia in a short-bore magnet (1.5 T ACS NT; Philips, The Netherlands) using an ultrafast T2-weighted single-shot LoLo TSE sequence and a T1-weighted gradient-echo sequence. The frozen liver tissue was depicted accurately on fast T2- and T1-weighted sequences, providing precise delineation of the ablated tissue volume. On follow-up postcontrast MR controls, the cryolesions appeared avascular. They decreased in size compared with the initially frozen volume down to 70% at a 2-week follow-up. Histologically, a coagulation necrosis with a close correlation to the MR follow-up examinations was objectified. No cryotherapy-related complications occurred. J. Magn. Reson. Imaging 2001;13:50-56. Copyright 2001 Wiley-Liss, Inc.

L21 ANSWER 11 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:80581 BIOSIS
 DN PREV200100080581
 TI Chemical strategies for the global analysis of protein function.
 AU Cravatt, Benjamin F. (1); Sorenson, Erik J.
 CS (1) Department of Cell Biology, Skaggs Institute for Chemical Biology, Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA, 92037: cravatt@scripps.edu USA
 SO Current Opinion in Chemical Biology, (December, 2000) Vol. 4, No. 6, pp. 663-668. print.
 ISSN: 1367-5931.
 DT General Review
 LA English
 SL English

L21 ANSWER 12 OF 25 MEDLINE DUPLICATE 9
 AN 2000079544 MEDLINE
 DN 20079544 PubMed ID: 10611275
 TI Activity-based protein profiling: the serine hydrolases.

AU Liu Y; Patricelli M P; Cravatt B F
 CS The Skaggs Institute for Chemical Biology, Department of Cell Biology, the Scripps Research Institute, La Jolla, CA 92037, USA.
 SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Dec 21) 96 (26) 14694-9.
 Journal code: PV3; 7505876. ISSN: 0027-8424.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 200001
 ED Entered STN: 20000204
 Last Updated on STN: 20000204
 Entered Medline: 20000127
 AB With the postgenome era rapidly approaching, new strategies for the functional analysis of proteins are needed. To date, **proteomics** efforts have primarily been confined to recording variations in protein level rather than activity. The ability to profile classes of proteins on the basis of changes in their activity would greatly accelerate both the assignment of protein function and the identification of potential pharmaceutical targets. Here, we describe the chemical synthesis and utility of an active-site directed probe for visualizing dynamics in the expression and function of an entire enzyme family, the serine hydrolases. By reacting this probe, a biotinylated fluorophosphonate referred to as FP-biotin, with crude tissue extracts, we quickly and with high sensitivity detect numerous serine hydrolases, many of which display tissue-restricted patterns of expression. Additionally, we show that FP-biotin labels these proteins in an activity-dependent manner that can be followed kinetically, offering a powerful means to monitor dynamics simultaneously in both protein function and expression.

L21 ANSWER 13 OF 25 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2000:135106 BIOSIS
 DN PREV200000135106
 TI Identification of essential residues involved in the glutamate binding pocket of the group II metabotropic glutamate receptor as **probed** by the radiolabelled selective agonist, (3H)-LY354740.
 AU Malherbe, P. (1); Broger, C. (1); Ohresser, S. (1); Adam, G. (1); Stadler, H. (1); Kemp, J. A. (1); Mutel, V. (1)
 CS (1) Pharma Division, Preclinical CNS Research, F. Hoffmann-La Roche Ltd, CH-4070, Basel Switzerland
 SO Society for Neuroscience Abstracts., (1999) Vol. 25, No. 1-2, pp. 975. Meeting Info.: 29th Annual Meeting of the Society for Neuroscience. Miami Beach, Florida, USA October 23-28, 1999 Society for Neuroscience . ISSN: 0190-5295.
 DT Conference
 LA English
 SL English

L21 ANSWER 14 OF 25 MEDLINE
 AN 1999201581 MEDLINE
 DN 99201581 PubMed ID: 10101365
 TI [Experimental MRI-controlled cryotherapy of the brain with almost real-time imaging by radial k-space scanning]. Experimentelle MR-gesteuerte Kryotherapie des Gehirns mit nahezu Echtzeitdarstellung durch radiale k-Raum-Abtastung.
 AU Tacke J; Speetzen R; Schorn R; Glowinski A; Grosskortenhaus S; Adam G; Rasche V; Rau G; Gunther R W
 CS Klinik fur Radiologische Diagnostik, Medizinische Einrichtungen der RWTH Aachen.. tacke@rad.rwth-aachen.de

SO ROFO. FORTSCHRITTE AUF DEM GEBIETE DER RONTGENSTRAHLEN UND DER NEUEN
 BILDGEBENDEN VERFAHREN, (1999 Feb) 170 (2) 214-7.
 Journal code: A7R; 9112114. ISSN: 0936-6652.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA German
 FS Priority Journals
 EM 199904
 ED Entered STN: 19990426
 Last Updated on STN: 19990426
 Entered Medline: 19990415
 AB PURPOSE: To test radial k-space scanning by MR fluoroscopy to guide and control MR-guided interstitial cryotherapy of the healthy pig brain.
 METHODS: After MR tomographic planning of the approach, an MR-compatible experimental cryotherapy probe of 2.7 mm diameter was introduced through a 5 mm burr hole into the right frontal brain of five healthy pigs. The freeze-thaw cycles were imaged using a T1-weighted gradient echo sequence with radial k-Space scanning in coronal, sagittal, and axial directions. RESULTS: The high temporal resolution of the chosen sequence permits a continuous representation of the freezing process with good image quality and high contrast between ice and unfrozen brain parenchyma. Because of the interactive conception of the sequence the layer plane could be chosen as desired during the measurement. Ice formation was sharply demarcated, spherically configurated, and was free of signals. Its maximum diameter was 13 mm. CONCLUSIONS: With use of the novel, interactively controllable gradient echo sequence with radial k-space scanning, guidance of the intervention under fluoroscopic conditions with the advantages of MRT is possible. MR-guided cryotherapy allows a minimally-invasive, precisely dosable focal tissue ablation.

L21 ANSWER 15 OF 25 MEDLINE
 AN 1999284532 MEDLINE
 DN 99284532 PubMed ID: 10354485
 TI The genotype and epigenotype synergize to diversify the spatial pattern of expression of the imprinted H19 gene.
 AU Lin W L; He X B; Svensson K; Adam G; Li Y M; Tang T W; Paldi A; Pfeifer S; Ohlsson R
 CS Department of Animal Development and Genetics, Uppsala University, Norbyvagen 18A, S-752 36, Uppsala, Sweden.
 SO MECHANISMS OF DEVELOPMENT, (1999 Apr) 82 (1-2) 195-7.
 Journal code: AXF; 9101218. ISSN: 0925-4773.
 CY Ireland
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199908
 ED Entered STN: 19990816
 Last Updated on STN: 19990816
 Entered Medline: 19990802
 AB Little is known of how the genetic background effects the phenomenon of genomic imprinting. The H19 gene belongs to a cluster of imprinted genes on human chromosome 11. Here we show that the alternative splicing of a human H19 transcript is genotype-specific. Moreover, this variant transcript, which lacks exon 4, is either not found at all, is widely expressed or is confined to extra-villous cytotrophoblasts in first trimester placenta, depending on a combination of the genotype and the sex of the transmitting parent.

L21 ANSWER 16 OF 25 MEDLINE
 AN 1998158355 MEDLINE

DN 98158355 PubMed ID: 9498590
 TI MR-guided interstitial cryotherapy of the liver with a novel,
 nitrogen-cooled cryoprobe.
 AU Tacke J; Adam G; Speetzen R; Brucksch K; Bucker A; Heshel I;
 Prescher A; van Vaals J J; Hunter D W; Rau G; Gunther R W
 CS Department of Diagnostic Radiology, University of Technology, Aachen,
 Germany.
 SO MAGNETIC RESONANCE IN MEDICINE, (1998 Mar) 39 (3) 354-60.
 Journal code: MHR; 8505245. ISSN: 0740-3194.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199804
 ED Entered STN: 19980507
 Last Updated on STN: 19980507
 Entered Medline: 19980430
 AB The purpose of the study was to test a newly developed, MR-compatible,
 liquid nitrogen-cooled cryoprobe. The **probe** has an outer
 diameter of 3.5 mm and was specifically developed for percutaneous,
 MR-guided, interstitial cryotherapy. The **probe** was inserted
 percutaneously into the livers of 10 rabbits. The cryotherapy procedure
 was monitored with a surface coil in a 1.5 Tesla magnet using a gradient
 echo sequence. Follow-up examinations were performed 3 and 7 days after
 the freezing procedure using T1- and T2-weighted spin echo sequences. At 7
 days the animals were sacrificed and the cryolesions were examined
 histologically. The cryoprobe enabled artifact-free MR imaging of the
 "iceball" formation during freezing of the rabbit liver. After 1 min of
 freezing, the iceball at the tip of the **probe** showed an average
 maximum diameter of 10.8 mm. No bleeding complications were observed
 during or after the freezing procedure. Histologic examination 7 days
 after cryotherapy confirmed that the liver lesions were the same size as
 had been predicted by the images of the acute iceball. This new,
 percutaneously inserted, MR-compatible, liquid-nitrogen cooled cryoprobe
 allows accurate, artifact-free MR imaging of interstitial cryotherapy.

L21 ANSWER 17 OF 25 MEDLINE
 AN 1998247275 MEDLINE
 DN 98247275 PubMed ID: 9586183
 TI [Fiber optic measurements with the Bilitec **probe** for quantifying
 bile reflux after aboral stomach resection].
 Fiberoptische Messungen mit einer Bilitec-Sonde zur Quantifizierung des
 Gallerefluxes nach aboraler Magenresektion.
 AU Kronert T; Kahler G; Adam G; Scheele J
 CS Abteilung Allgemeine und Viszerale Chirurgie, Friedrich-Schiller-
 Universitat Jena.
 SO ZENTRALBLATT FUR CHIRURGIE, (1998) 123 (3) 239-44.
 Journal code: Y5I; 0413645. ISSN: 0044-409X.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA German
 FS Priority Journals
 EM 199807
 ED Entered STN: 19980723
 Last Updated on STN: 19980723
 Entered Medline: 19980715
 AB Nonphysiological alkaline reflux after partial gastrectomy may produce a
 range of gastrointestinal disorders. The Bilitec **probe** is a
 fibroptic sensor that, for the first time, makes in vivo measurement of
 this reflux possible, by assay of spectrophotometric absorption of

bilirubin. We studied 20 patients who had undergone partial gastrectomy for benign peptic ulcer disease. Ten patients had Billroth II reconstruction and ten had Roux-en-Y reconstruction. In the Roux-en-Y Group we found almost complete control of symptoms and no objective evidence of alkaline reflux as measured by the Bilitec probe. In the Billroth II group we detected by the fiberoptic sensor significant bile reflux into the stomach remnant. Based on these results we recommend Roux-en-Y gastrojejunostomy as the method of choice for reconstruction after distal gastric resection.

- L21 ANSWER 18 OF 25 MEDLINE
 AN 96194043 MEDLINE
 DN 96194043 PubMed ID: 8631262
 TI Allele-specific *in situ* hybridization (ASISH) analysis: a novel technique which resolves differential allelic usage of H19 within the same cell lineage during human placental development.
 AU Adam G I; Cui H; Miller S J; Flam F; Ohlsson R
 CS Department of Animal Development and Genetics, University of Uppsala, Sweden.
 SO DEVELOPMENT, (1996 Mar) 122 (3) 839-47.
 Journal code: ECW; 8701744. ISSN: 0950-1991.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199607
 ED Entered STN: 19960715
 Last Updated on STN: 19960715
 Entered Medline: 19960702
 AB Precursory studies of H19 transcription during human foetal development have demonstrated maternally derived monoallelic expression. Analyses in extra-embryonic tissues, however, have been more equivocal, with discernible levels of expression of the paternal allele of H19 documented in the first trimester placenta. By refining the *in situ* hybridization technique we have developed an assay to enable the functional imprinting status of H19 to be determined at the cellular level. This assay involves the use of oligonucleotide DNA probes that are able to discriminate between allelic RNA transcripts containing sequence polymorphisms. Biallelic expression of H19 is confined to a subpopulation of cells of the trophoblast lineage, the extravillous cytotrophoblast, while the mesenchymal stroma cells maintain the imprinted pattern of monoallelic expression of H19 throughout placental development. This data demonstrates that the low level of paternal H19 expression previously detected in normal human placenta is not due to a random loss of functional imprinting, but appears to result from a developmentally regulated cell type-specific activation of the paternal allele. In addition, biallelic expression of H19 does not seem to affect the functional imprinting of the insulin-like growth factor II gene, which is monoallelically expressed at relatively high levels in the extra-villous cytotrophoblasts. These results imply that the allelic usage of these two genes in normal human placental development may not be directly analogous to the situation previously documented in the mouse embryo.
- L21 ANSWER 19 OF 25 MEDLINE
 AN 91160512 MEDLINE
 DN 91160512 PubMed ID: 1848176
 TI Negative regulation of transcription of the *Saccharomyces cerevisiae* catalase T (CTT1) gene by cAMP is mediated by a positive control element.
 AU Belazzi T; Wagner A; Wieser R; Schanz M; Adam G; Hartig A; Ruis H

CS Institut fur Allgemeine Biochemie, Universitat Wien, Austria.
 SO EMBO JOURNAL, (1991 Mar) 10 (3) 585-92.
 Journal code: EMB; 8208664. ISSN: 0261-4189.
 CY ENGLAND: United Kingdom
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199104
 ED Entered STN: 19910505
 Last Updated on STN: 19910505
 Entered Medline: 19910415
 AB Transcription of the CTT1 (catalase T) gene of *Saccharomyces cerevisiae* is controlled by oxygen via heme, by nutrients via cAMP and by heat shock. Nitrogen limitation triggers a rapid, cycloheximide-insensitive derepression of the gene. Residual derepression in a cAMP-nonresponsive mutant with attenuated protein kinase activity (bcyl tpk1w tpk2 tpk3) demonstrates the existence of an alternative, cAMP-independent nutrient signaling mechanism. Deletion analysis using CTT1-lacZ fusion genes revealed the contribution of multiple control elements to derepression, not all of which respond to the cAMP signal. A positive promoter element responding to negative control by cAMP was inactivated by deletion of a DNA region between base pairs -340 and -364. Upstream fragments including this element confer negative cAMP control to a LEU2-lacZ fusion gene. Northern analysis of CTT1 expression in the presence or absence of heme, in RAS2+ (high cAMP) and ras2 mutant (low cAMP) strains and in cells grown at low temperature (23 degrees C) and in heat-shocked cells (37 degrees C) shows that CTT1 is only induced to an appreciable extent when at least two of the three factors contributing to its expression (oxidative stress signaled by heme, nutrient starvation (low cAMP) and heat stress) activate the CTT1 promoter.

L21 ANSWER 20 OF 25 MEDLINE DUPLICATE 10
 AN 91007766 MEDLINE
 DN 91007766 PubMed ID: 2210741
 TI Cystic fibrosis in Greece: typing with DNA **probes** and identification of the common molecular defect.
 AU Balassopoulou A; Loukopoulos D; Kollia P; Devoto M; **Adam G**; Arvanitakis S; Hadjisevastou H
 CS First Department of Medicine, University of Athens Medical School, Laikon Hospital, Greece.
 SO HUMAN GENETICS, (1990 Sep) 85 (4) 393-4.
 Journal code: GED; 7613873. ISSN: 0340-6717.
 CY GERMANY: Germany, Federal Republic of
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199011
 ED Entered STN: 19910117
 Last Updated on STN: 19910117
 Entered Medline: 19901121
 AB The relative frequency of the delta F508 mutation in the Greek population is 54.1%; this is similar to that reported in other Southern European populations and contrasts with the considerably higher frequencies encountered in Northern Europe and North America. The low frequency is in agreement with the linkage disequilibrium already reported between cystic fibrosis and haplotype B in this country. In contrast to the common association of pancreatic insufficiency with the homozygous delta F508 genotype, the present study revealed two homozygous children with no evidence of pancreatic failure.

L21 ANSWER 21 OF 25 MEDLINE
 AN 90077431 MEDLINE
 DN 90077431 PubMed ID: 2574150
 TI Haplotypes in cystic fibrosis patients with or without pancreatic insufficiency from four European populations.
 AU Devoto M; De Benedetti L; Seia M; Piceni Sereni L; Ferrari M; Bonduelle M L; Malfroot A; Lissens W; Balassopoulou A; Adam G; +
 CS Laboratorio Genetica Molecolare, Istituto G. Gaslini, Genoa, Italy.
 SO GENOMICS, (1989 Nov) 5 (4) 894-8.
 Journal code: GEN; 8800135. ISSN: 0888-7543.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 199001
 ED Entered STN: 19900328
 Last Updated on STN: 19950206
 Entered Medline: 19900125
 AB We examined the allele and haplotype frequencies of five polymorphic DNA markers in 355 European cystic fibrosis (CF) patients (from Belgium, the German Democratic Republic, Greece, and Italy) who were divided into two groups according to whether they were or not taking supplementary pancreatic enzymes. The level of linkage disequilibrium between each polymorphism and the CF mutation varied among the different populations; there was no significant association between KM.19 and CF in the Greek population. The distributions of alleles and haplotypes derived from the polymorphisms revealed by probes KM.19 and XV.2c were always different in patients with or without pancreatic insufficiency (PI) in all the populations studied. In particular, among 32 patients without PI, only 9 (or 28%) were homozygous for the KM.19-XV.2c = 2-1 haplotype (which was present in 73% of all the CF chromosomes in our sample) compared to 162 of 252 patients (or 64%) with PI. These findings are consistent with the hypothesis that pancreatic insufficiency or sufficiency may be determined by different mutations at the CF locus.

L21 ANSWER 22 OF 25 MEDLINE DUPLICATE 11
 AN 88332299 MEDLINE
 DN 88332299 PubMed ID: 2843603
 TI Microtubule-associated cyclic AMP-dependent protein kinase in Drosophila melanogaster.
 AU Adam G; Friedrich P
 CS Institute of Enzymology, Biological Research Center, Hungarian Academy of Sciences, Budapest.
 SO JOURNAL OF NEUROCHEMISTRY, (1988 Oct) 51 (4) 1014-22.
 Journal code: JAV; 2985190R. ISSN: 0022-3042.
 CY United States
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198810
 ED Entered STN: 19900308
 Last Updated on STN: 19900308
 Entered Medline: 19881019
 AB Microtubules were prepared from head extracts of the adult fruit fly, *Drosophila melanogaster*, by one-step, taxol-assisted polymerization. The microtubular fraction displayed cyclic AMP-dependent protein kinase (protein kinase A) activity, as witnessed by endogenous protein phosphorylation and by protein kinase assay. Microtubule-bound protein kinase A amounts to 4-5% of total soluble kinase activity, which is almost an order of magnitude less than in mammals. The high-molecular-weight

microtubule-associated protein-2 (MAP-2), the main binding species for protein kinase A in mammalian brain microtubules, is not detectable in the fly system by protein staining and immunoblotting with anti-pig MAP-2 serum, as well as by hybridization of fly DNA with a cDNA **probe** for human MAP-2. Cyclic AMP removes a major part of the regulatory (R) subunit of the enzyme from Drosophila microtubules, as demonstrated by enzyme assay, autophosphorylation of R subunit, and quantitating cyclic AMP binding sites. It is proposed that permanently elevated cyclic AMP levels may elute protein kinase A from crucial intracellular binding sites, thereby interfering with signal transduction.

L21 ANSWER 23 OF 25 MEDLINE DUPLICATE 12
 AN 88059471 MEDLINE
 DN 88059471 PubMed ID: 3680462
 TI Lectins as **probes** for the assay of rhabdovirus infections in plants.
 AU Adam G; Heegard P; Bog-Hansen T C; Mundry K W
 CS Institute for Biology, University of Stuttgart, F.R.G.
 SO JOURNAL OF VIROLOGICAL METHODS, (1987 Sep) 17 (3-4) 263-75.
 Journal code: HQR; 8005839. ISSN: 0166-0934.
 CY Netherlands
 DT Journal; Article; (JOURNAL ARTICLE)
 LA English
 FS Priority Journals
 EM 198801
 ED Entered STN: 19900305
 Last Updated on STN: 19900305
 Entered Medline: 19880115
 AB Thirteen different, biotinylated plant lectins were tested for their ability to recognize specifically the glycoproteins of the two different plant rhabdoviruses potato yellow dwarf virus and eggplant mottled dwarf virus. All viruses were propagated on the same plant host species, Nicotiana rustica L. The lectin-binding to the viral proteins was tested after electrophoretic separation and transfer to nitrocellulose membranes. Besides purified virus also partially pure virus preparations were used for the tests, in order to determine the specificity. The lectins had been selected for specificities to either one of the following monosaccharides: mannose, glucose, galactose, N-acetyl-D-galactosamine, N-acetyl-D-glucosamine and fucose. In the test panel of thirteen lectins, seven were found to react with the viral glycoproteins. Among these, four (LCA, VFA, PSA, Con A) belonged to the mannosyl- or glycosyl-specific group. However, these four lectins reacted also with other host proteins when partially pure virus preparations were used as samples. The other three lectins (GSA2b, STA, WGA) were specific for N-acetyl-D-glucosamine and detected almost exclusively the viral glycoproteins. Two of these lectins, STA and WGA, were extremely suitable for virus-specific assays, since they did not react with glycoproteins in healthy controls that were identical or comparable in their electrophoretic mobility with the rhabdovirus glycoproteins. No binding to viral glycoproteins was observed with galactose-, N-acetyl-galactosamine- and fucose-specific lectins. The assay for rhabdovirus glycoproteins in plants with the lectins was approximately 8-16 times less sensitive than with virus-specific antibodies.

L21 ANSWER 24 OF 25 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1985-081585 [14] WPIDS
 DNN N1985-061098
 TI Sifting machine with wind channel and gas stream - has weighing zone, **probes** and evaluator to adjust gas stream for efficient sorting.
 DC P43

IN ADAM, G; HAING, B; RUDOLF, W; SCHLINZIG, E
 PA (FORT) VEB KOMB FORTSCHRIT
 CYC 1
 PI DD 216124 A 19841128 (198514)*
 ADT DD 216124 A DD 1983-251027 19830518
 PRAI DD 1983-251027 19830518
 AB DD 216124 A UPAB: 19930925
 The sifting machine has at the end of a wind sifting channel a taring zone formed by at least one **probe** in each of various planes. These **probes** are connected to a control device and the control device is in connection with a regulator for the gas stream in the wind sifting channel.

The whirled-up materials pass the **probes** of the taring zone which take up the vibrations and direct them to the control device. The values are compared to see whether the proportion of materials are sufficiently whirled up for separation and whether the loss of faulty-ejected materials lies within the given limits.

USE - The intensity of the gas stream can now be selected to ensure sufficient material separation whilst faulty discharge of materials is reduced to a minimum.

L21 ANSWER 25 OF 25 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1982-A3430J [48] WPIDS
 TI Temp. variation measuring circuit for thermometric analysis - includes compensation loops for ambient temp. and fluid heat capacitance.
 DC S03
 IN ADAM, G; FARKAS, F; FEHER, I; KOVACS, F; LANYI, M; SAJO, I;
 SOLYMAR, K; UJVARI, J
 PA (ALUT) ALUMINIUMIPARI TERVEZO; (MAAL-N) MAGYAR ALUMINIUMIPA; (VASI)
 VASIPARI KI
 CYC 4
 PI DE 3214947 A 19821125 (198248)* 26p
 FR 2505519 A 19821112 (198251)
 HU 27028 T 19830928 (198345)
 AT 8201442 A 19910215 (199112)
 PRAI HU 1981-1195 19810507
 AB DE 3214947 A UPAB: 19930915

The circuit uses a temp. **probe**, dipping into the fluid and coupled via a temp. measuring device to one input of a difference current circuit. The output of the latter is fed via a storage stage to an adding or subtracting stage for combining the supplied voltage or current value with an electronic reference value dependant on the material.

The combined signal is compared with the direct output signal from the difference current circuit, with the obtained difference signal fed to a process control stage and/or a display unit. The junction between the temp. measuring device and the difference current circuit is coupled to a second comparator receiving a signal from a second temp. measuring **probe**, to supply an output corresp. to the fluid heat capacitance to the adding or subtracting stage.

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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 13 March 2002 (20020313/ED)

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(FILE 'BIOSIS' ENTERED AT 12:40:51 ON 18 MAR 2002)
DEL HIS Y
L1 1809 S PROTEOM?
L2 132709 S PROBE#
L3 162261 S SCREEN?
L4 76196 S (BIOACTIV? OR BIO? (2W) ACTIV?)
L5 22271 S TARGET? (5A) (PROTEIN# OR MOL# OR MOLEC? OR ENZYM?)
L6 50 S L1 AND L2
L7 12 S L6 AND (L3 OR L4)
L8 3 S L5 AND L6
L9 12 S L7 OR L8
L10 106667 S LIGAND#
L11 2089161 S PROTEIN# OR ENZYM?
L12 2250 S L2 AND L10 AND L11
L13 43 S L12 AND L5
L14 15136 S FUNCTION? (3A) (GR## OR GROUP#)
L15 2 S L13 AND L14
L16 1004 S ACTIVIT? (4A) L2
L17 0 S L13 AND L16
L18 2 S L13 AND CONJUGAT?
L19 3 S L13 AND LINK?
L20 19 S L8 OR L9 OR L15 OR L18 OR L19

FILE 'BIOSIS' ENTERED AT 12:58:50 ON 18 MAR 2002

=> d bib ab it 1-19

L20 ANSWER 1 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2002:193718 BIOSIS
DN PREV200200193718
TI Concept and prototype of **protein-ligand** docking
simulator with force feedback technology.
AU Nagata, Hiroshi (1); Mizushima, Hiroshi (1); Tanaka, Hiroshi
CS (1) National Cancer Center Research Institute, 5-1-1, Tsukiji, Chuo-ku,
Tokyo, 104-0045: hi-nagata@kddilabs.co.jp, hmizushi@ncc.go.jp,
tanaka@cim.tmd.ac.jp Japan
SO Bioinformatics (Oxford), (January, 2002) Vol. 18, No. 1, pp. 140-146.
print.
ISSN: 1367-4803.
DT Article
LA English
AB A novel concept for a **protein-ligand** docking simulator
using Virtual Reality (VR) technologies, in particular the tactile sense
technology, was designed and a prototype was developed. Most conventional
docking simulators are based on numerical differential calculations of the
total energy between a **protein** and a **ligand**. However,
the basic concept of our method differs from that of conventional
simulators. Our design utilizes the force between a **ligand** and a
protein instead of the total energy. The most characteristic

function of the system is its ability to enable the user to 'touch' and sense the electrostatic potential field of a **protein** molecule. The user can scan the surface of a **protein** using a globular **probe**, which is given an electrostatic charge, and is controlled by a force feedback device. The electrostatic force between the **protein** and the **probe** is calculated in real time and immediately fed back into the force feedback device. The user can easily search interactively for positions where the **probe** is strongly attracted to the force field. Such positions can be regarded as candidate sites where **functional groups of ligands** corresponding to the **probe** can bind to the **target protein**. Certain limitations remain; for example, only twenty **protein** atoms can be used to generate the electrostatic field. Furthermore, the system can only use globular **probes**, preventing drug molecules or small chemical groups from being simulated. These limitations are the result of our insufficient computer resources. However, our prototype system has the potential to become a novel application method as well as being applicable to conventional VR technologies, especially to force feedback technologies.

- IT Major Concepts
 Biochemistry and Molecular Biophysics; Computer Applications
 (Computational Biology)
- IT Chemicals & Biochemicals
protein
- IT Methods & Equipment
 force feedback device: laboratory equipment; software: computer software; tactile sense technology: analytical method, computer method; virtual reality technology: analytical method, computer method
- IT Miscellaneous Descriptors
 electrostatics; **protein-ligand** interaction

- L20 ANSWER 2 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2002:193674 BIOSIS
 DN PREV200200193674
 TI A one-bead, one-stock solution approach to chemical genetics: Part 2.
 AU Clemons, Paul A.; Koehler, Angela N.; Wagner, Bridget K.; Sprigings, Timothy G.; Spring, David R.; King, Randall W.; Schreiber, Stuart L. (1); Foley, Michael A.
 CS (1) Howard Hughes Medical Institute, Harvard University, Cambridge, MA, 02138: sls@slsiris.harvard.edu, mfoley@infinitypharm.com USA
 SO Chemistry & Biology (London), (December, 2001) Vol. 8, No. 12, pp. 1183-1195. <http://www.elsevier.nl/inca/publications/store/6/0/1/2/8/1/index.htm>. print.
 ISSN: 1074-5521.
 DT Article
 LA English
 AB Background: Chemical genetics provides a systematic means to study biology using small molecules to effect spatial and temporal control over protein function. As complementary approaches, phenotypic and **proteomic screens** of structurally diverse and complex small molecules may yield not only interesting individual **probes** of biological function, but also global information about small molecule collections and the interactions of their members with biological systems. Results: We report a general high-throughput method for converting high-capacity beads into arrayed stock solutions amenable to both phenotypic and **proteomic assays**. Polystyrene beads from diversity-oriented syntheses were arrayed individually into wells. Bound compounds were cleaved, eluted, and resuspended to generate 'mother plates' of stock solutions. The second phase of development of our technology platform includes optimized cleavage and elution conditions, a novel bead arraying method, and robotic distribution of stock solutions of small molecules into 'daughter plates' for direct use in chemical genetic assays. This library formatting strategy enables what we refer to as annotation

screening, in which every member of a library is annotated with biological assay data. This phase was validated by arraying and screening 708 members of an encoded 4320-member library of structurally diverse and complex dihydropyrancarboxamides. Conclusions: Our 'one-bead, multiple-stock solution' library formatting strategy is a central element of a technology platform aimed at advancing chemical genetics. Annotation **screening** provides a means for biology to inform chemistry, complementary to the way that chemistry can inform biology in conventional ('investigator-initiated') small molecule screens.

- IT Major Concepts
 Biochemistry and Molecular Biophysics; Equipment, Apparatus, Devices and Instrumentation; Methods and Techniques
- IT Chemicals & Biochemicals
 dihydropyrancarboxamides; protein: function
- IT Methods & Equipment
 annotation **screening**: Molecular Biology Techniques and Chemical Characterization, **screening** method; bead arraying method: Preparatory and General Laboratory Techniques, analytical method; chemical genetic assays: Molecular Biology Techniques and Chemical Characterization, genetic method; diversity-oriented synthesis: Synthetic Techniques, synthetic method; high-capacity beads: laboratory equipment; high-throughput method: Molecular Biology Techniques and Chemical Characterization, analytical method; phenotypic **screen**: Molecular Biology Techniques and Chemical Characterization, **screening** method; polystyrene beads: laboratory equipment; **proteomic screen**: Molecular Biology Techniques and Chemical Characterization, **screening** method
- IT Miscellaneous Descriptors
 chemical genetics; one-bead, one-stock solution approach; optimized cleavage conditions; optimized elution conditions

- L20 ANSWER 3 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2002:167561 BIOSIS
 DN PREV200200167561
 TI Generating addressable protein microarrays with PROfusionTM covalent mRNA-protein fusion technology.
 AU Weng, Shawn; Gu, Ke; Hammond, Philip W.; Lohse, Peter; Rise, Cecil; Wagner, Richard W.; Wright, Martin C.; Kuimelis, Robert G. (1)
 CS (1) Phylos, Inc., 128 Spring Street, Lexington, MA, 02421:
 rkkuimelis@phylos.com USA
 SO Proteomics, (January, 2002) Vol. 2, No. 1, pp. 48-57. print.
 ISSN: 1615-9853.
 DT Article
 LA English
 AB An mRNA-protein fusion consists of a polypeptide covalently linked to its corresponding mRNA. These species, prepared individually or en masse by *in vitro* translation with a modified mRNA conjugate (the PROfusionTM process), link phenotype to genotype and enable powerful directed evolution schemes. We have exploited the informational content of the nucleic acid component of the mRNA-protein fusion to create an addressable protein microarray that self-assembles via hybridization to surface-bound DNA capture **probes**. The nucleic acid component not only directs the mRNA-protein fusion to the proper coordinate of the microarray, but also positions the protein in a uniform orientation. We demonstrate the feasibility of this protein chip concept with several mRNA-protein fusions, each possessing a unique peptide epitope sequence. These addressable proteins could be visualized on the microarray both by autoradiography and highly specific monoclonal antibody binding. The anchoring of the protein to the chip surface is surprisingly robust, and the system is sensitive enough to detect sub-attomole quantities of displayed protein without signal amplification. Such protein arrays should

be useful for functional screening in massively parallel formats, as well as other applications involving immobilized peptides and proteins.

IT Major Concepts

Methods and Techniques; Molecular Genetics (Biochemistry and Molecular Biophysics)

IT Chemicals & Biochemicals

DNA; DNA capture probes; DNA microarrays: preparation, uses; mRNA [messenger RNA]: analysis; messenger RNA-polypeptide fusions: applications, preparation; messenger RNA-protein fusions: applications, preparation; monoclonal antibodies; nucleic acids; peptide epitopes; polypeptides; protein microarrays: preparation, uses; proteins: molecular analysis

IT Methods & Equipment

HPLC [high performance liquid chromatography]: liquid chromatography, purification method; PCR [polymerase chain reaction]: DNA amplification, in situ recombinant gene expression detection, molecular method, sequencing techniques; fluorescence laser scanning: Molecular Biology Techniques and Chemical Characterization, analytical method; phosphorimaging analysis: Imaging Techniques, analytical method; protein chips/biochips: laboratory equipment, preparation, uses

IT Miscellaneous Descriptors

PROfusion covalent messenger RNA-protein fusion technology: applications; genome sequencing projects: methodologies; proteomics

L20 ANSWER 4 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:542807 BIOSIS

DN PREV200100542807

TI The cloning of human genes using cDNA phage display and small-molecule chemical probes.

AU Savinov, Sergey N.; Austin, David J. (1)

CS (1) Department of Chemistry, Sterling Chemical Laboratory, Yale University, New Haven, CT, 06520: david.austin@yale.edu USA

SO Combinatorial Chemistry & High Throughput Screening, (November, 2001) Vol. 4, No. 7, pp. 593-597. print.

ISSN: 1386-2073.

DT Article

LA English

SL English

AB The cloning of genes based on protein function has become a powerful tool for protein discovery and should play an important role in proteomics in general. We have recently reported a technique for the functional identification of protein targets by combining traditional affinity chromatography with cDNA phage display. This procedure, referred to as display cloning, directly couples biologically active natural products to the gene of their protein cellular target. We now report the cloning of a human gene, the alpha domain of F1 ATP synthase, using a synthetic scaffold molecule which serves as a prototype for a diverse chemical library. The ability to select genes from cDNA libraries using probes from combinatorial libraries would greatly increase the number of small molecule/protein interactions that can be identified. This method might prove valuable in furthering our understanding of biology and its application toward drug development.

IT Major Concepts

Chemistry; Genetics; Methods and Techniques

IT Methods & Equipment

complementary DNA phage display: genetic method; small-molecule chemical probes: analytical method

IT Miscellaneous Descriptors

human gene cloning

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L20 ANSWER 5 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:497022 BIOSIS

DN PREV200100497022

TI Simplified sample preparation method for protein identification by matrix-assisted laser desorption/ionization mass spectrometry: In-gel digestion on the **probe** surface.

AU Stensballe, Allan; Jensen, Ole Norregaard (1)

CS (1) Department of Biochemistry and Molecular Biology, University of Southern Denmark, Odense University, Campusvej 55, DK-5230, Odense M: jensen@bmb.sdu.dk Denmark

SO European Journal of Mass Spectrometry, (2001) Vol. 7, No. 2, pp. 111-121. print.

ISSN: 1469-0667.

DT Article

LA English

SL English

AB Identification and detailed characterization of complex mixtures of proteins separated by polyacrylamide gel electrophoresis (PAGE) require optimized and robust methods for interfacing electrophoretic techniques to mass spectrometry. Peptide mapping by matrix-assisted laser desorption/ionization (MALDI) time-of-flight mass spectrometry (TOF MS) is used as the first protein **screening** method in many laboratories because of its inherent simplicity, mass accuracy, sensitivity and relatively high sample throughput. We present a simplified sample preparation method for MALDI MS that enables in-gel digestion of protein samples directly on the MALDI MS metal **probe**. Removal of detergent and reagents as well as protein reduction and S-alkylation were performed prior to cutting of protein samples from the polyacrylamide gel slab. The general utility of this approach was demonstrated by on-**probe** digestion and MALDI MS peptide mapping of femtomole amounts of standard proteins isolated by sodium dodecyl sulfate (SDS) PAGE. A representative set of 47 human proteins obtained from a silver stained two-dimensional electrophoretic gel was analyzed by the new method and resulted in a success rate for protein identification similar to that obtained by the traditional protocols for in-gel digestion and MALDI peptide mass mapping of human proteins, i.e. approximately 60%. The overall performance of the novel on-**probe** digestion method is comparable with that of the standard in-gel sample preparation protocol while being less labor-intensive and more cost-effective due to minimal consumption of reagents, enzymes and consumables. Preliminary data obtained on a MALDI quadrupole-TOF tandem mass spectrometer demonstrated the utility of the on-**probe** digestion protocol for peptide mass mapping and peptide sequencing on this instrument. Automation of the on-**probe** protein digestion procedure and its combination with automated MALDI tandem mass spectrometry should be advantageous in **proteomics** research aimed at the systematic identification and analysis of large sets of proteins from electrophoretic gels.

IT Major Concepts

Biochemistry and Molecular Biophysics; Methods and Techniques

IT Chemicals & Biochemicals

bovine beta-casein: Sigma, identification, peptide mapping, separation;
bovine serum albumin: Sigma, identification, peptide mapping,
separation; ovalbumin: Sigma, identification, peptide mapping,
separation; proteins: identification, peptide mapping, separation

IT Methods & Equipment

API QSTAR Pulsar quadrupole time-of-flight mass spectrometer: MDS Sciex, laboratory equipment; Bio-Rad Mini-PROTEAN II electrophoresis

system: Bio-Rad, laboratory equipment; REFLEX reflectron time-of-flight mass spectrometer: Bruker Daltonics, laboratory equipment; matrix-assisted laser/desorption ionization mass spectrometry: analytical method, spectroscopic techniques: CB; polyacrylamide gel electrophoresis: gel electrophoresis, separation method; probe surface in-gel digestion: Preparatory and General Laboratory Techniques, sample preparation method

- L20 ANSWER 6 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:491354 BIOSIS
 DN PREV200100491354
 TI Profiling the specific reactivity of the **proteome** with non-directed chemical libraries.
 AU Adam, Gregory C. (1); Cravatt, Benjamin F.; Sorensen, Erik J.
 CS (1) Department of Chemistry, Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA, 92037: gadam@scripps.edu USA
 SO Abstracts of Papers American Chemical Society, (2001) Vol. 222, No. 1-2, pp. BIOL84. print.
 Meeting Info.: 222nd National Meeting of the American Chemical Society Chicago, Illinois, USA August 26-30, 2001 American Chemical Society . ISSN: 0065-7727.
 DT Conference
 LA English
 SL English
 AB Through **screening** the **proteome** with chemical **probes** bearing functionalities common to organic synthesis but underutilized in biology, proteins or classes of proteins susceptible to new forms of inactivation may be discovered. A library of biotinylated sulfonates was synthesized and its members applied to complex **proteomes** under conditions that distinguish patterns of specific protein reactivity. Individual sulfonates exhibited unique profiles of **proteome** reactivity that in extreme cases appeared completely orthogonal to one another. Targets of the tagged sulfonate library include members of multiple structurally and mechanistically distinct enzyme families. Progress towards understanding the mechanisms by which the sulfonate **probes** react with their discrete **enzyme** **targets** will be reported. These data reveal that a non-directed approach towards probing the chemical reactivity of the **proteome** can readily identify compounds possessing selective and unanticipated **biological activities**.
 IT Major Concepts
 Biochemistry and Molecular Biophysics; Cell Biology
 IT Chemicals & Biochemicals
 biotinylated sulfonate library; chemical **probes**; protein: reactivity patterns
 IT Methods & Equipment
 biotinylated sulfonate synthesis: synthetic method; **proteome** screening: **screening** method
 IT Miscellaneous Descriptors
 proteome; Meeting Abstract
- L20 ANSWER 7 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:477440 BIOSIS
 DN PREV200100477440
 TI Simplified sample preparation method for protein identification by matrix-assisted laser desorption/ionization mass spectrometry: In-gel digestion on the **probe** surface.
 AU Stensballe, Allan; Jensen, Ole Norregaard (1)
 CS (1) Department of Biochemistry and Molecular Biology, University of Southern Denmark, Odense University, Campusvej 55, DK-5230, Odense M: jenseno@bmb.sdu.dk Denmark
 SO Proteomics, (August, 2001) Vol. 1, No. 8, pp. 955-966. print.
 ISSN: 1615-9853.

DT Article
 LA English
 SL English
 AB Identification and detailed characterization of complex mixtures of proteins separated by polyacrylamide gel electrophoresis (PAGE) require optimized and robust methods for interfacing electrophoretic techniques to mass spectrometry. Peptide mapping by matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF-MS) is used as the first protein **screening** method in many laboratories because of its inherent simplicity, mass accuracy, sensitivity and relatively high sample through-put. We present a simplified sample preparation method for MALDI-MS that enables in-gel digestion of protein samples directly on the MALDI-MS metal **probe**. Removal of detergent and reagents as well as protein reduction and S-alkylation were performed prior to cutting of protein samples from the polyacrylamide gel slab. The general utility of this approach was demonstrated by on-**probe** digestion and MALDI-MS peptide mapping of femtomole amounts of standard proteins isolated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis. A representative of 47 human proteins obtained from a silver stained two-dimensional electrophoretic gel was analyzed by the new method and resulted in a success rate for protein identification similar to that obtained by the traditional protocols for in-gel digestion and MALDI peptide mass mapping of human proteins, i.e. approximately 60%. The overall performance of the novel on-**probe** digestion method is comparable with that of the standard in-gel sample preparation protocol while being less labour intensive and more cost-effective due to minimal consumption of reagents, enzymes and consumables. Preliminary data obtained on a MALDI quadrupole-TOF tandem mass spectrometer demonstrated the utility of the on-**probe** digestion protocol for peptide mass mapping and peptide sequencing on this instrument. Automation of the on-**probe** protein digestion procedure and its combination with automated MALDI tandem mass spectrometry should be advantageous in **proteomics** research aimed at the systematic identification and analysis of large sets of proteins from electrophoretic gels.

IT Major Concepts
 Enzymology (Biochemistry and Molecular Biophysics); Computer Applications (Computational Biology); Equipment, Apparatus, Devices and Instrumentation; Methods and Techniques

IT Chemicals & Biochemicals
 2,5-dihydroxybenzoic acid: Aldrich; SDS; acetonitrile: Fisher Scientific; alpha-cyano-4-hydroxycin-namic acid: Aldrich; bovine beta-casein: Sigma; bovine serum albumin: Sigma; ovalbumin: Sigma; protein; trypsin: Promega

IT Methods & Equipment
 GPMW 4.0 software: Light-house Data, computer software; Inspector software V2.2.12: MDS **Proteomics**, computer software; Milli-Q system: Millipore, laboratory equipment; Q-TOF hybrid instrument: Micromass, laboratory equipment; SDS-polyacrylamide gel electrophoresis: Electrophoretic Techniques, analytical method; in-gel digestion: Molecular Biology Techniques and Chemical Characterization, biochemical method; matrix-assisted laser desorption/ionization mass spectrometry: Spectrum Analysis Techniques, analytical method; matrix-assisted laser desorption/ionization mass spectrometry metal **probe**: laboratory equipment; matrix-assisted laser desorption/ionization quadrupole-time of flight mass spectrometer: MDS Sciex, laboratory equipment; matrix-assisted laser desorption/ionization-time of flight mass spectrometry: Spectrum Analysis Techniques, analytical method; nanoelectrospray needle: MDS **Proteomics**, laboratory equipment; polyacrylamide gel electrophoresis [PAGE]: Electrophoretic Techniques, gel electrophoresis, separation method; polyacrylamide gel slab: laboratory equipment; protein identification: Molecular Biology Techniques and Chemical Characterization, identification method; ready-for-use Poros

R2 nanoscale desalting column: laboratory equipment; sample preparation: Preparatory and General Laboratory Techniques, laboratory method; two-dimensional electrophoretic gel: laboratory equipment

RN 490-79-9 (2,5-DIHYDROXYBENZOIC ACID)
 75-05-8 (ACETONITRILE)
 28166-41-8 (ALPHA-CYANO-4-HYDROXYCIN-NAMIC ACID)
 9002-07-7 (TRYPSIN)

L20 ANSWER 8 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:458877 BIOSIS
 DN PREV200100458877
 TI Surrogate ligands in a **proteomics**-based antibacterial program with targets of unknown biological function.
 AU Christensen, J. (1)
 CS (1) Karo Bio USA, Durham, NC USA
 SO International Journal of Antimicrobial Agents, (June, 2001) Vol. 17, No. Supplement 1, pp. S52. print.
 Meeting Info.: 22nd International Congress of Chemotherapy Amsterdam, Netherlands June 30-July 03, 2001
 ISSN: 0924-8579.

DT Conference
 LA English
 SL English
 IT Major Concepts
 Molecular Genetics (Biochemistry and Molecular Biophysics);
 Pharmacology
 IT Chemicals & Biochemicals
 BioKeys: peptide **probe**; enzymes; peptide **probe**; phage display library; surrogate ligands
 IT Miscellaneous Descriptors
 high throughput **screening** assay development;
 proteomics-based antibacterial program; Meeting Abstract

L20 ANSWER 9 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:390263 BIOSIS
 DN PREV200100390263
 TI Oxidative **protein** cross-linking reactions involving L-tyrosine in transforming growth factor-beta1-stimulated fibroblasts.
 AU Larios, Jose M.; Budhiraja, Rohit; Fanburg, Barry L.; Thannickal, Victor J. (1)
 CS (1) Pulmonary and Critical Care Division, New England Medical Center, 750 Washington St., NEMC 257, Boston, MA, 02111: vthannickal@lifespan.org USA
 SO Journal of Biological Chemistry, (May 18, 2001) Vol. 276, No. 20, pp. 17437-17441. print.
 ISSN: 0021-9258.

DT Article
 LA English
 SL English
 AB The mechanisms by which **ligand**-stimulated generation of reactive oxygen species in nonphagocytic cells mediate biologic effects are largely unknown. The profibrotic cytokine, transforming growth factor-beta1 (TGF-beta1), generates extracellular hydrogen peroxide (H2O2) in contrast to intracellular reactive oxygen species production by certain mitogenic growth factors in human lung fibroblasts. To determine whether tyrosine residues in fibroblast-derived extracellular matrix (ECM) **proteins** may be **targets** of H2O2-mediated dityrosine-dependent cross-linking reactions in response to TGF-beta1, we utilized fluorophore-labeled tyramide, a structurally related phenolic compound that forms dimers with tyrosine, as a **probe** to detect such reactions under dynamic cell culture conditions. With this approach, a distinct pattern of fluorescent labeling that seems to **target** ECM **proteins** preferentially was observed in TGF-beta1-treated cells but not in control cells. This reaction required the presence of a

heme peroxidase and was inhibited by catalase or diphenyliodonium (a flavoenzyme inhibitor), similar to the effect on TGF-beta1-induced dityrosine formation. Exogenous addition of H₂O₂ to control cells that do not release extracellular H₂O₂ produced a similar fluorescent labeling reaction. These results support the concept that, in the presence of heme peroxidases *in vivo*, TGF-beta1-induced H₂O₂ production by fibroblasts may mediate oxidative dityrosine-dependent cross-linking of ECM protein(s). This effect may be important in the pathogenesis of human fibrotic diseases characterized by overexpression/activation of TGF-beta1.

IT Major Concepts

Biochemistry and Molecular Biophysics; Methods and Techniques

IT Parts, Structures, & Systems of Organisms
fibroblast

IT Chemicals & Biochemicals

L-tyrosine: Sigma; extracellular matrix proteins; heme
peroxidase: catalyst; hydrogen peroxide; reactive oxygen species;
transforming growth factor-beta-1: R&D Systems

IT Methods & Equipment

cell culture: Preparatory and General Laboratory Techniques, cell
culture method

IT Miscellaneous Descriptors
molecular mechanism

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

human (Hominidae)

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 60-18-4 (L-TYROSINE)

9003-99-0 (HEME PEROXIDASE)

7722-84-1 (HYDROGEN PEROXIDE)

L20 ANSWER 10 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:329040 BIOSIS

DN PREV200100329040

TI Applications of mass spectrometry in the study of inborn errors of metabolism.

AU Clayton, P. T. (1)

CS (1) Biochemistry, Endocrinology and Metabolism Unit, Institute of Child Health, 30 Guilford Street, London, WC1N 1EH: p.clayton@ich.ucl.ac.uk UK

SO Journal of Inherited Metabolic Disease, (April, 2001) Vol. 24, No. 2, pp. 139-150. print.

ISSN: 0141-8955.

DT Article

LA English

SL English

AB During the twentieth century, and particularly in its last decade, there have been major advances in mass spectrometry (MS). As a result, MS remains one of the most powerful tools for the investigation of genetic metabolic disease. Analysis of organic acids by gas chromatography-mass spectrometry (GC-MS) and analysis of acylcarnitines by tandem mass spectrometry are still leading to the discovery of new disorders. Tandem mass spectrometry is increasingly being used for neonatal screening. New methods for lipid analysis have opened up the fields of inborn errors of cholesterol synthesis, of bile acid synthesis and of leukotriene synthesis. The latest developments in MS allow it to be used for determination of the amino acid sequence and posttranslational modifications of proteins. There are still some major hurdles to be overcome, but soon it should be possible to detect mutant proteins directly rather than by cDNA or genomic DNA analysis. Measurement of which proteins are overexpressed and underexpressed ('proteomics') should provide further information on the pathogenesis of complications of

inborn errors, e.g. hepatic cirrhosis. The use of stable isotopes in conjunction with MS allows us to **probe** metabolic pathways. As an example, evidence is presented to support the contention that vitamin E and its oxidation product are catabolized by peroxisomal beta-oxidation. Mass spectrometry also has a major role in monitoring new forms of treatment for inborn errors.

IT Major Concepts
 Metabolism; Methods and Techniques

IT Diseases
 inborn error of bile acid synthesis: congenital disease, metabolic disease; inborn error of cholesterol synthesis: congenital disease, metabolic disease; inborn error of leukotriene synthesis: congenital disease, metabolic disease; inborn error of metabolism: congenital disease, metabolic disease

IT Chemicals & Biochemicals
 acylcarnitines; bile acid; cholesterol; leukotrienes; proteins: amino acid sequences, posttranslational modification; vitamin E

IT Methods & Equipment
 gas chromatography-mass spectrometry: analytical method; mass spectrometry: analytical method, spectroscopic techniques: CB, spectroscopic techniques: CT; tandem mass spectrometry: analytical method

IT Miscellaneous Descriptors
 peroxisomal-beta-oxidation

ORGN Super Taxa
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name
 human (Hominidae)

ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Primates; Vertebrates

RN 57-88-5 (CHOLESTEROL)
 1406-18-4 (VITAMIN E)

L20 ANSWER 11 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 2001:302761 BIOSIS
 DN PREV200100302761
 TI Probing the surface of eukaryotic cells using combinatorial toxin libraries.
 AU Bray, Mark R.; Bisland, Stuart; Perampalam, Subodini; Lim, Wai-May; Gariepy, Jean (1)
 CS (1) Princess Margaret Hospital, Ontario Cancer Institute, 610 University Avenue, Rm. 7-117, Toronto, Ontario, M5G 2M9: gariepy@uhnres.utoronto.ca Canada
 SO Current Biology, (1 May, 2001) Vol. 11, No. 9, pp. 697-701. print.
 ISSN: 0960-9822.
 DT Article
 LA English
 SL English
 AB The success of **proteomics** hinges in part on the development of approaches able to map receptors on the surface of cells. One strategy to **probe** a cell surface for the presence of internalized markers is to make use of Shiga-like toxin 1 (SLT-1), a ribosome-inactivating protein that kills eukaryotic cells. SLT-1 binds to the glycolipid globotriaosylceramide, which acts as a shuttle, allowing the toxin to be imported and routed near ribosomes. We investigated the use of SLT-1 as a structural template to create combinatorial libraries of toxin variants with altered receptor specificity. Since all SLT-1 variants retain their toxic function, this property served as a search engine enabling us to identify mutants from these libraries able to kill target cells expressing internalizable receptors. Random mutations were introduced in two discontinuous loop regions of the SLT-1 receptor binding subunit. Minimal searches from **screening** 600 bacterial colonies randomly picked from an SLT-1 library identified toxin mutants able to kill cell lines

resistant to the wild-type toxin. One such mutant toxin was shown to bind to a new receptor on these cell lines by flow cytometry. Toxin libraries provide a strategy to delineate the spectrum of receptors on eukaryotic cells.

IT Major Concepts

Biochemistry and Molecular Biophysics; Membranes (Cell Biology);
Methods and Techniques

IT Parts, Structures, & Systems of Organisms
cell; cell surfaceIT Chemicals & Biochemicals
Shiga-like toxin-1; receptorIT Methods & Equipment
combinatorial toxin library: analytical method; flow cytometry:
analytical method

ORGN Super Taxa

Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGN Organism Name

CAMA-1 cell line (Hominidae); PC-3 cell line (Hominidae)

ORGN Organism Superterms

Animals; Chordates; Humans; Mammals; Primates; Vertebrates

L20 ANSWER 12 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:174149 BIOSIS

DN PREV200100174149

TI Profiling the specific reactivity of the **proteome** with
non-directed activity-based **probes**.

AU Adam, Gregory C.; Cravatt, Benjamin F.; Sorensen, Erik J. (1)

CS (1) Department of Chemistry, Skaggs Institute for Chemical Biology,
Scripps Research Institute, 10550 N. Torrey Pines Rd., La Jolla, CA,
92037: cravatt@scripps.edu, sorensen@scripps.edu USA

SO Chemistry & Biology (London), (January, 2001) Vol. 8, No. 1, pp. 81-95.
print.

ISSN: 1074-5521.

DT Article

LA English

SL English

AB Background: The field of **proteomics** aims to characterize dynamics in protein function on a global level. However, several classes of proteins, in particular low abundance proteins, remain difficult to characterize using standard **proteomics** technologies. Recently, chemical strategies have emerged that profile classes of proteins based on activity rather than quantity, thereby greatly facilitating the analysis of low abundance constituents of the **proteome**. Results: In order to expand the classes of proteins susceptible to analysis by activity-based methods, we have synthesized a library of biotinylated sulfonate esters and applied its members to complex **proteomes** under conditions that distinguish patterns of specific protein reactivity. Individual sulfonates exhibited unique profiles of **proteome** reactivity that in extreme cases appeared nearly orthogonal to one another. A robustly labeled protein was identified as a class I aldehyde dehydrogenase and shown to be irreversibly inhibited by members of the sulfonate library. Conclusions: Through **screening** the **proteome** with a non-directed library of chemical **probes**, diverse patterns of protein reactivity were uncovered. These **probes** labeled **protein targets** based on properties other than abundance, circumventing one of the major challenges facing contemporary **proteomics** research. Considering further that the **probes** were found to inhibit a **target enzyme**'s catalytic activity, the methods described herein should facilitate the identification of compounds possessing both selective **proteome** reactivities and novel **bioactivities**.

IT Major Concepts

Biochemistry and Molecular Biophysics; Methods and Techniques

IT Chemicals & Biochemicals
 aldehyde dehydrogenases: analysis; enzymes: analysis; molecular probes: non-directed activity-based, preparation, uses; proteome: analysis, specific activity profiling

IT Methods & Equipment
 NMR spectroscopy: analytical method, spectroscopic techniques: CB; mass spectrometry: analytical method, spectroscopic techniques: CB

IT Miscellaneous Descriptors
 biotechnology; proteomics: applications; proteomics technologies: applications

RN 9028-86-8 (ALDEHYDE DEHYDROGENASES)

L20 ANSWER 13 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2001:127376 BIOSIS

DN PREV200100127376

TI Cloning arbuscule-related genes from mycorrhizas.

AU Burleigh, S. (1)

CS (1) Centre for Plant Microbe Symbioses, Plant Biology and Biogeochemistry Department, Risoe National Laboratory, DK-4000, Roskilde: stephen.burleigh@risoe.dk Denmark

SO Plant and Soil, (2000) Vol. 226, No. 2, pp. 287-292. print.
 ISSN: 0032-079X.

DT Article

LA English

SL English

AB Until recently little was known about the identity of the genes expressed in the arbuscules of mycorrhizas, due in part to problems associated with cloning genes from the tissues of an obligate symbiont. However, the combination of advanced molecular techniques, innovative use of the materials available and fortuitous cloning has resulted in the recent identification of a number of arbuscule-related genes. This article provides a brief summary of the genes involved in arbuscule development, function and regulation, and the techniques used to study them. Molecular techniques include differential screening, differential display and screening with heterologous probes, and can involve the use of mycorrhizal plant mutants. New technologies such as proteome analysis are also discussed.

IT Major Concepts
 Molecular Genetics (Biochemistry and Molecular Biophysics); Infection

IT Parts, Structures, & Systems of Organisms
 hyphae

IT Methods & Equipment
 differential display: genetic method; differential screening: genetic method; heterologous probe screening: genetic method

ORGN Super Taxa
 Phycomycetes: Fungi, Plantae

ORGN Organism Name
 arbuscular mycorrhizal fungi (Phycomycetes)

ORGN Organism Superterms
 Fungi; Microorganisms; Nonvascular Plants; Plants

L20 ANSWER 14 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 2000:356522 BIOSIS

DN PREV200000356522

TI Developing a dynamic pharmacophore model for HIV-1 integrase.

AU Carlson, Heather A. (1); Masukawa, Kevin M.; Rubins, Kathleen; Bushman, Fredric D.; Jorgensen, William L.; Lins, Roberto D.; Briggs, James M.; McCammon, J. Andrew

CS (1) Department of Chemistry and Biochemistry, University of California, San Diego, 9500 Gilman Drive, La Jolla, CA, 92093-0365 USA

SO Journal of Medicinal Chemistry, (June 1, 2000) Vol. 43, No. 11, pp. 2100-2114. print.

DT Article
 LA English
 SL English
 AB We present the first receptor-based pharmacophore model for HIV-1 integrase. The development of "dynamic" pharmacophore models is a new method that accounts for the inherent flexibility of the active site and aims to reduce the entropic penalties associated with binding a ligand. Furthermore, this new drug discovery method overcomes the limitation of an incomplete crystal structure of the target protein. A molecular dynamics (MD) simulation describes the flexibility of the uncomplexed protein. Many conformational models of the protein are saved from the MD simulations and used in a series of multi-unit search for interacting conformers (MUSIC) simulations. MUSIC is a multiple-copy minimization method, available in the BOSS program; it is used to determine binding regions for probe molecules containing functional groups that complement the active site. All protein conformations from the MD are overlaid, and conserved binding regions for the probe molecules are identified. Those conserved binding regions define the dynamic pharmacophore model. Here, the dynamic model is compared to known inhibitors of the integrase as well as a three-point, ligand-based pharmacophore model from the literature. Also, a "static" pharmacophore model was determined in the standard fashion, using a single crystal structure. Inhibitors thought to bind in the active site of HIV-1 integrase fit the dynamic model but not the static model. Finally, we have identified a set of compounds from the Available Chemicals Directory that fit the dynamic pharmacophore model, and experimental testing of the compounds has confirmed several new inhibitors.
 IT Major Concepts
 Enzymology (Biochemistry and Molecular Biophysics);
 Pharmaceuticals (Pharmacology)
 IT Diseases
 HIV infection [human immunodeficiency virus infection]: immune system disease, viral disease
 IT Chemicals & Biochemicals
 HIV-1 integrase [human immunodeficiency virus-1 integrase]: pharmacophore model; protein: target, uncomplexed
 IT Alternate Indexing
 HIV Infections (MeSH)
 IT Miscellaneous Descriptors
 molecular dynamics simulation
 ORGN Super Taxa
 Retroviridae: Animal Viruses, Viruses, Microorganisms
 ORGN Organism Name
 HIV-1 [human immunodeficiency virus 1] (Retroviridae)
 ORGN Organism Superterms
 Animal Viruses; Microorganisms; Viruses
 L20 ANSWER 15 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1998:491189 BIOSIS
 DN PREV199800491189
 TI Hydrophobic residues in the C-terminal region of S100A1 are essential for target protein binding but not for dimerization.
 AU Osterloh, Dirk; Ivanenkov, Vasily V.; Gerke, Volker (1)
 CS (1) Inst. Med. Biochem., ZMBE, Univ. Muenster, D-48149 Muenster Germany
 SO Cell Calcium, (Aug., 1998) Vol. 24, No. 2, pp. 137-151.
 ISSN: 0143-4160.
 DT Article
 LA English
 AB S100 proteins are a family of small dimeric proteins characterized by two EF hand type Ca²⁺ binding motifs which are flanked by unique N- and C-terminal regions. Although shown unequivocally in only a

few cases S100 **proteins** are thought to function by binding to, and thereby regulating, cellular **target proteins** in a Ca²⁺ dependent manner. To describe for one member of the family, S100A1, structural requirements underlying **target protein** binding, we generated specifically mutated S100A1 derivatives and characterized their interaction with the a subunit of the actin capping **protein** CapZ shown here to represent a direct binding partner for S100A1. Chemical cross-linking, ligand blotting and fluorescence emission spectroscopy reveal that removal of, or mutations within, the sequence encompassing residues 88-90 in the unique C-terminal region of S100A1 interfere with binding to CapZalpha and to TRTK-12, a synthetic CapZalpha peptide. The S100A1 sequence identified contains a cluster of three hydrophobic residues (Phe-88, Phe-89 and Trp-90) at least one of which - as revealed by qualitative phenyl Sepharose binding and hydrophobic fluorescent **probe** spectroscopy - is exposed on the **protein** surface of Ca²⁺ bound S100A1. As homologous hydrophobic residues in the closely related S100B **protein** were shown by NMR spectroscopy of Ca²⁺-free S100B dimers to provide intersubunit contacts (Kilby RM., van Eldik L.J., Roberts G.C.K. The solution structure of the bovine S100B dimer in the calcium-free state. Structure 1996; 4: 1041-1052; Drohat A.C., Amburgey J.C., Abildgaard F., Starich M.R., Baldissari D., Weber D.J. Solution structure of rat apo-S100B (beta beta) as determined by NMR spectroscopy. Biochemistry 1996; 35: 11577-11588), we characterized the physical state of the various S100A1 derivatives. Analytical gel filtration and chemical cross-linking show that dimer formation is not compromised in S100A1 mutants lacking residues 88-90 or containing specific amino acid substitutions in this sequence. Thus a cluster of hydrophobic residues in the C-terminal region of S100A1 is essential for **target protein** binding but dispensable for dimerization, a situation possibly met in other S100 **proteins** as well.

IT Major Concepts

Biochemistry and Molecular Biophysics

IT Chemicals & Biochemicals

S-100A1 **protein**: amino acid sequence, carboxyl-terminal hydrophobic residues, **target protein** binding, dimerization

L20 ANSWER 16 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1998:356066 BIOSIS

DN PREV199800356066

TI A new photoactivatable reagent capable of transferring a radiolabel to **target proteins**. Application to the human growth hormone-rat liver prolactin receptor interaction.

AU Masckauchan, Nestor T. H.; Delfino, Jose M. (1); Fernandez, Horacio N.

CS (1) IQUIFIB, Fac. Farm. y Bioquim., Junin 956, 1113 Buenos Aires Argentina

SO Bioconjugate Chemistry, (July-Aug., 1998) Vol. 9, No. 4, pp. 507-511.

ISSN: 1043-1802.

DT Article

LA English

AB A new photoactivatable cross-linking reagent, 1-(2'-dithiopyridyl)-2-(5'-azidosalicylamido)ethane (ASDPE), was synthesized. This **probe** can be easily labeled with ¹²⁵I in the azidosalicylamido ring and contains an activated disulfide bridge. After reaction of (¹²⁵I)ASDPE with **proteins**, the radiolabeled moiety of the **probe** becomes attached to cysteine residues. Upon partial reduction of human growth hormone (hGH) with dithiothreitol, its C-terminal disulfide bond between residues 182 and 189 was cleaved and the nascent thiol groups were modified with (¹²⁵I)ASDPE to yield (¹²⁵I)ASET-hGH (1-(thio-hGH)-2-(3'-(¹²⁵I)iodo-5'-azidosalicylamido)ethane). After binding of this hormone derivative to rat liver microsomes, followed by photolysis and subsequent reduction of disulfide bridges, the specific transfer of the radiolabeled moiety to

prolactin receptor (PRL-R) was achieved. Partial purification of the radiolabeled receptor by size exclusion chromatography was performed. We anticipate that (125I)ASDPE will be generally useful in pursuing structural and functional studies of target proteins which interact specifically with protein ligands.

IT Major Concepts
 Methods and Techniques
 IT Parts, Structures, & Systems of Organisms
 rat liver prolactin receptor
 IT Chemicals & Biochemicals
 human growth hormone; 1-(2'-dithiopyridyl)-2-(5'-azidosalicylamido)ethane [ASDPE]: photoactivatable cross-linking reagent, synthesis
 IT Methods & Equipment
 protein purification; size exclusion chromatography;
 isolation method, purification method, liquid chromatography; NMR:
 imaging techniques, spectroscopic techniques: CB; 1-(2'-dithiopyridyl)-2-(5'-azidosalicylamido)ethane synthesis: Synthesis/Modification Techniques, synthetic method
 IT Miscellaneous Descriptors
 growth hormone-prolactin receptor interaction
 RN 9002-62-4 (PROLACTIN)

L20 ANSWER 17 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1998:347059 BIOSIS
 DN PREV199800347059
 TI Human rab11a: Transcription, chromosome mapping and effect on the expression levels of host GTP-binding proteins.
 AU Gromov, Pavel S. (1); Celis, Julio E.; Hansen, Claus; Tommerup, Niels; Gromova, Irina; Madsen, Peder
 CS (1) Dep. Med. Biochem., Aarhus Univ., Ole Worms Alle 170, Build. 170, DK-8000 Aarhus Denmark
 SO FEBS Letters, (June 16, 1998) Vol. 429, No. 3, pp. 359-364.
 ISSN: 0014-5793.
 DT Article
 LA English
 AB Rab11a is a member of the rab-branch of the ras-like small GTP-binding protein superfamily that is associated with both constitutive and regulated secretory pathways. Using a direct procedure for cDNA cloning of small ras-related GTPases, that is based on the screening of eukaryotic cDNA expression libraries using (α -32P)GTP as a probe, we have isolated two cDNA clones encoding rab11a. Both clones share identical coding sequences, but differ in the length and sequence of their 3' untranslated regions (3'-UTR). Northern blot hybridisation analysis of various human tissues revealed indeed two mRNA species with lengths of 1.0 and 2.3 kb, respectively. Sequence analysis of the cDNAs identified two different putative polyadenylation signals (AATAAA) at positions 927 and 2302 of the larger transcript. In addition, the 3'-UTR of the larger transcript exhibited several AU-rich elements (ARE) that are believed to control gene expression by regulating the rate of mRNA degradation. Southern blots of human DNA digested with several rare restriction enzymes, and separated by pulse-field gel electrophoresis, yielded the same macro-restriction fragment pattern when hybridised with probes that discriminate between the two transcripts. Taken together, these findings imply that the two mRNA species originate from a single gene, which we have mapped to 15q21.3-q22.31, by the use of different polyadenylation sites. As expected, both rab11a-cDNAs yielded the same protein product when transiently expressed in COS-1 cells, and surprisingly, upregulated the proteome expression profile (de novo synthesis or posttranslational modification of preexisting proteins) of a few other, yet unknown GTP-binding proteins.
 IT Major Concepts

IT Molecular Genetics (Biochemistry and Molecular Biophysics)
 IT Chemicals & Biochemicals
 complementary DNA; messenger RNA; rab11a: transcription; GTP-binding
 protein: expression; GTPase: small ras-related
 IT Sequence Data
 AF000231: DDBJ, EMBL, GenBank, nucleotide sequence
 IT Methods & Equipment
 chromosome mapping: genetic method
 IT Miscellaneous Descriptors
 gene expression; sequence alignment
 ORGN Super Taxa
 Cercopithecidae: Primates, Mammalia, Vertebrata, Chordata, Animalia;
 Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
 ORGN Organism Name
 human (Hominidae); COS-1 (Cercopithecidae)
 ORGN Organism Superterms
 Animals; Chordates; Humans; Mammals; Nonhuman Mammals; Nonhuman
 Primates; Nonhuman Vertebrates; Primates; Vertebrates
 RN 9059-32-9 (GTPASE)

L20 ANSWER 18 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1986:420323 BIOSIS
 DN BA82:95857
 TI DRUG TARGETING TO THE LIVER WITH LACTOSYLATED ALBUMINS DOES THE
 GLYCOPROTEIN TARGET THE DRUG OR IS THE DRUG TARGETING THE GLYCOPROTEIN.
 AU VAN DER SLUIJS P; BOOTSMA H P; POSTEMA B; MOOLENAAR F; MEIJER D K F
 CS DEP. PHARM. THER., DRUG DESIGN AND DEV. PROGRAM, UNIV. OF GRONINGEN, ANT.
 DEUSINGLAAN 2, NL-9713 AW GRONINGEN, THE NETHERLANDS.
 SO HEPATOLOGY (BALTIMORE), (1986) 6 (4), 723-728.
 CODEN: HPTLD9. ISSN: 0270-9139.
 FS BA; OLD
 LA English
 AB The isolated perfused rat liver preparation was employed to study hepatic
 disposition of the model drug-carrier **conjugate**
 fluorescein-lactosylated albumin (F-LnHSA) with special reference to the
 influence of the organic anion fluorescein on liver cell specificity of
 the endocytosed neoglycoprotein. Hepatic clearance of fluoresceinated
 neoglycoproteins was significantly faster than clearance of radioiodinated
 neoglycoproteins. Perfusion clearance of F-L7HSA and F-L25HSA could not
 completely be inhibited by a dose of 10 mg asialoorosomucoid that
 saturates the hepatocyte receptor-mediated endocytic process. From these
 data, we inferred an additional hepatic uptake mechanism, competing with
 the Ashwell-receptor-mediated internalization of galactose-terminated
 glycoproteins. Clearance experiments with fluoresceinated 125I-human serum
 albumin in the presence of the polyanionic **probe** dextran sulfate
 revealed a nearly complete (.apprx. 90%) inhibition of hepatic uptake,
 while also a pronounced effect was obtained with colloidal carbon. These
 data point to nonparenchymal cell uptake of fluoresceinated
 protein via interaction with scavenger receptors. In wash-out
 studies, it was shown that about 25% of **ligand** sequestered by
 sinusoidal liver cells escaped degradation and recycled to the perfusion
 medium. Our results show that care should be taken in the use of
 neoglycoproteins as drug carriers to hepatocytes, since a load of only 2
 to 3 moles fluorescein per mole neoglycoprotein considerably affects
 intrahepatic distribution. The relative contribution of nonparenchymal
 cell uptake by coupling of acidic drugs to the neoglycoproteins is very
 probably inversely related to the number of exposing galactose groups per
 molecule neoglycoprotein. This phenomenon of "inversed
 targeting" could therapeutically both be useful or detrimental,
 dependent on the spectrum of cell types that should be reached by the
 drug.
 IT Miscellaneous Descriptors
 RAT FLUORESCEIN-LACTOSYLATED ALBUMIN CONJUGATE PHARMACEUTICAL

ADJUNCT-DRUG GASTROINTESTINAL-DRUG DRUG CARRIER RADIO IODINE HEPATIC
CLEARANCE ASIALOOROSOMUCOID INHIBITION RECEPTOR-MEDIATED
INTERNALIZATION INTRAHEPATIC DRUG DISTRIBUTION ACIDIC DRUG COUPLING
INVERSED TARGETING PHARMACOKINETICS PHARMACODYNAMICS

RN 7553-56-2 (IODINE)

L20 ANSWER 19 OF 19 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

AN 1985:377445 BIOSIS

DN BA80:47437

TI MORPHOLOGICAL ANALYSIS OF **LIGAND** UPTAKE AND PROCESSING THE ROLE
OF MULTIVESICULAR ENDOSOMES AND COMPARTMENT OF UNCOUPLING OF RECEPTOR AND
LIGAND IN RECEPTOR-**LIGAND** PROCESSING.

AU HARDING C; LEVY M A; STAHL P

CS DEP. PHYSIOLOGY AND BIOPHYSICS, WASHINGTON UNIV. SCH. MED., 660 SOUTH
EUCLID AVE., ST. LOUIS, MO 63110, USA.

SO EUR J CELL BIOL, (1985) 36 (2), 230-238.
CODEN: EJCBDN. ISSN: 0171-9335.

FS BA; OLD

LA English

AB The receptor-mediated endocytosis and intracellular processing of transferrin and mannose receptor **ligands** were investigated in bone marrow-derived macrophages, fibroblasts and reticulocytes. Mannosylated bovine serum albumin (BSA) **conjugated** to colloidal Au (Au-man-BSA) or colloidal Au-transferrin (AuTf) were used to trace **ligand** processing in these cells. These **ligands** appeared to be processed by mechanisms similar to those observed previously with other mannose receptor and galactose receptor **ligand probes**. After uptake via coated pits and coated vesicles, Au-man-BSA appeared in small uncoated vesicles and tubular structures and was transferred to large, sometimes multivesicular endosomes (MVEs), which sometimes had arm-like protrusions reminiscent of CURL (compartment of uncoupling of receptor and **ligand**). Initially these structures became increasingly multivesicular, but during longer incubations the inclusion vesicles appeared to disintegrate to leave a denser, amorphous lumen. Inclusion vesicle disintegration may result from the introduction of lysosomal **enzymes** into these structures. These results suggest a model for differential receptor-**ligand** and **ligand-ligand** sorting. As suggested membrane constituents may be recycled to the plasma membrane from the arms of CURL. Receptor-bound **ligands**, such as transferrin, would also recycle. The luminal contents, including dissociated **ligands**, other soluble **proteins** and inclusion vesicles (containing some membrane **proteins**), would **target** to lysosomes. This would result in the lysosomal degradation of any membrane **proteins** that were incorporated in the inclusion vesicle membranes.

IT Miscellaneous Descriptors

BOVINE SERUM ALBUMIN BONE MARROW DERIVED MACROPHAGE FIBROBLAST
RETICULOCYTE SOLUBLE PROTEIN INCLUSION VESICLES LYSOSMAL
DEGRADATION **ENZYMES**

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FILE 'WPIDS' ENTERED AT 12:30:54 ON 18 MAR 2002

L1 104 S PROTEOM?
L2 70043 S PROBE?
L3 195974 S SCREEN?
L4 24325 S BIOACTIV? OR BIO? (3A) ACTIV?
L5 18626 S LIGAND#
L6 19136 S FUNCTIONAL (3A) (GR## OR GROUP#)
L7 3785 S TARGET? (5A) (PROTEIN# OR MOL## OR MOLECUL? OR ENZYM?)
L8 27 S L1 AND L2
L9 21 S L8 AND (L3 OR L4 OR L5 OR L6 OR L7)
L10 93156 S PROTEIN#
L11 62726 S ENZYM?
L12 17 S L9 AND (L10 OR L11)
L13 139982 S L10 OR L11
L14 7739 S L13 AND L2
L15 68 S L6 AND L14
L16 68 S L15 AND (L2 OR L3)
L17 15 S L15 AND (L3 OR L4)
L18 23 S L15 AND L5
L19 12 S L18 AND CONJUGAT?
L20 38 S L19 OR L17 OR L12
L21 17 S L20 AND L2 AND L5
L22 38 S L20 AND L2
L23 23 S L22 AND L6
L24 15 S L21 AND L23
L25 25 S L21 OR L23
L26 15 S L7 AND L20
L27 30 S L26 OR L25

FILE 'WPIDS' ENTERED AT 12:37:22 ON 18 MAR 2002

=> d .wp 1-30

L27 ANSWER 1 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2002-097640 [13] WPIDS
DNC C2002-030429

TI Novel human neurotransmitter transporter polypeptides and polynucleotides
for diagnosing, preventing or treating transport, neurological and
psychiatric disorders and for identifying modulators of therapeutic use.

DC B04 D16
 IN BAUGHN, M R; DING, L; ELLIOTT, V S; GANDHI, A R; HAFALIA, A; LAL, P;
 PATTERSON, C; RANKUMAR, J; SANJANWALA, M S; TRIBOULEY, C M; WALIA, N K;
 YAO, M G; YUE, H
 PA (INCY-N) INCYTE GENOMICS INC
 CYC 95
 PI WO 2001090148 A2 20011129 (200213)* EN 123p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
 DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
 LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD
 SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 ADT WO 2001090148 A2 WO 2001-US16283 20010517
 PRAI US 2000-228448P 20000727; US 2000-205518P 20000519; US 2000-213956P
 20000622; US 2000-215105P 20000628; US 2000-218947P 20000714
 AB WO 2001090148 A UPAB: 20020226
 NOVELTY - An isolated human neurotransmitter transporter polypeptide (I),
 (NTT) 1-6, comprising a sequence (S1) of 602, 730, 523, 649, 625 or 592
 amino acids defined in the specification, a naturally occurring
 polypeptide comprising an amino acid sequence 90% identical to (S1), a
biologically active or immunogenic fragment of (S1), is
 new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) an isolated polynucleotide (II) encoding (I) and comprising a
 sequence (S2) of 2168, 2709, 2958, 2135, 1997 or 2774 base pairs (bp)
 defined in the specification, a naturally occurring polynucleotide
 comprising a polynucleotide sequence 90% identical to (S2), a
 polynucleotide complementary to (II) or an RNA equivalent of (II);
 (2) a recombinant polynucleotide (III) comprising a promoter sequence
 operably linked to (II);
 (3) a cell transformed with (III);
 (4) a transgenic organism comprising (III);
 (5) method of producing (I);
 (6) an isolated antibody (IV) which specifically binds to (I);
 (7) an isolated polynucleotide comprising at least 60 contiguous
 nucleotides of (II);
 (8) detecting (M1) a target polynucleotide having the sequence of
 (II) in a sample, by:
 (a) hybridizing the sample with a **probe** comprising 20
 contiguous nucleotides comprising a sequence complementary to the target
 polynucleotide in the sample, where the **probe** specifically
 hybridizes to the target polynucleotide under conditions where a
 hybridization complex is formed between the **probe** and the target
 polynucleotide or its fragments, or by amplifying the target
 polynucleotide or its fragment by PCR; and
 (b) detecting the presence or absence of the hybridization complex or
 the amplified product, and, optionally, if present the amount of the
 complex or the amplified product;
 (9) an antibody (monoclonal) produced by using (I); and
 (10) a composition comprising (I), an agonist or antagonist compound
 identified using (I), (IV) or the above antibody.
 ACTIVITY - Antidiabetic; Antiparkinsonian; Antianginal;
 Neuroprotective; Nootropic; Antidepressant; Anticonvulsant; Neuroleptic;
 Antianemic; Ophthalmological; Antithyroid; Cerebroprotective;
 Tranquilizer; Vasotropic; Cytostatic; Antiarrhythmic; Dermatological;
 Antilipemic; Muscular-Gen; Antimicrobial; Cardiant; Antisickling;
 Antiinfertility; Endocrine-Gen.
 MECHANISM OF ACTION - Gene therapy; neurotransmitter transporter
 polypeptide modulator. No supporting data is given.
 USE - (I) is useful for **screening** a compound for
 effectiveness as an agonist or antagonist of (I), by exposing a sample

comprising (I) to a compound and detecting agonist or antagonist activity in the sample. (I), the identified agonist and antagonist are useful for treating a disease or condition associated with decreased or overexpression of functional NTT in a patient. (I) is useful for screening for a compound that modulates the activity of the polypeptide or that binds to the polypeptide. (I) is further useful as an immunogen for preparing polyclonal or monoclonal antibody by hybridoma technology. (II) is useful for screening a compound for effectiveness in altering expression of a target polynucleotide comprising the sequence of (II). A probe comprising at least 20 contiguous nucleotides of (II) is useful for assessing toxicity of a test compound, by treating a biological sample containing nucleic acids with the test compound, hybridizing the probe with nucleic acids of the treated biological sample to form a complex, quantifying the amount of hybridization complex and comparing the complex in the treated biological sample with the amount of complex in an untreated biological sample, where a difference in the amount of complex in the treated biological sample is indicative of toxicity of the test compound. (IV) is useful for detecting the presence of (I) and purifying (I) from a sample. (IV), optionally labeled is useful for diagnosing a condition or disease associated with expression of NTT in a subject or in a biological sample (all claimed). (I) and (II) and modulators of (I) are useful for diagnosis, treatment and prevention of transport, neurological and psychiatric disorders. Transport disorders include akinesia, amyotrophic lateral sclerosis, ataxia telangiectasia, cystic fibrosis, Becker's muscular dystrophy, diabetes mellitus, diabetes insipidus, myasthenia gravis, myocarditis, Parkinson's disease, prostate cancer; cardiac disorders associated with transport include angina, bradyarrhythmia, dermatomyositis, polymyositis, neurological disorders associated with transport include Alzheimer's disease, amnesia, bipolar disorder, dementia, depression, epilepsy, Tourette's disorder, schizophrenia, and other disorders associated with transport include neurofibromatosis, sickle cell anemia, Wilson's disease, cataracts, infertility, hyperglycemia, hypoglycemia, Graves' disease, goiter, Cushing's disease, hypercholesterolemia and cystinuria. Neurological disorders treatable include epilepsy, stroke, Huntington's disease, dementia, and other extrapyramidal disorder, motor neuron disorders, prion disease including kuru, metabolic disease of the nervous system, and other developmental disorders of the central nervous system, neuromuscular disorders, metabolic, endocrine and toxic myopathies, periodic paralysis, mental disorders including mood and anxiety. Psychiatric disorders include acute stress disorder, alcohol dependence, anorexia nervosa, anxiety, obsessive-compulsive disorder, panic disorder and sleep disorder. (II) is useful for creating knock in humanized animals or transgenic animals to model human disease and to detect and quantify gene expression in biopsied tissues in which expression of NTT is correlated with disease. (II) is also useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence and oligonucleotide primers derived from (II) are useful to detect single nucleotide polymorphisms. NTT, fragments of it and antibodies specific for NTT are useful as elements on a microarray which is useful to monitor or measure protein-protein interactions, drug-target interactions and gene expression profiles. Sequences of (I) are used to analyze the proteome of a tissue or cell type.

Dwg.0/0

L27 ANSWER 2 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2002-097342 [13] WPIDS
 CR 2002-010942 [68]
 DNN N2002-071955 DNC C2002-030233
 TI Composition useful for e.g. analyzing biological fluid comprises at least one covalent product of a target protein member and at least one activity based probe member of combinatorial chemical library.

DC A96 B04 D16 S03 T01
 IN ADAM, G; CRAVATT, B F; LOVATO, M; PATRICELLI, M; SORENSEN, E
 PA (SCRI) SCRIPPS RES INST
 CYC 94
 PI WO 2001077684 A2 20011018 (200213)* EN 119p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001027280 A 20011023 (200213)
 ADT WO 2001077684 A2 WO 2000-US34187 20001215; AU 2001027280 A AU 2001-27280
 20001215
 FDT AU 2001027280 A Based on WO 200177684
 PRAI US 2000-222532P 20000802; US 2000-195954P 20000410; US 2000-212891P
 20000620
 AB WO 200177684 A UPAB: 20020226
 NOVELTY - A composition comprising at least one covalent product of a
target protein member of a complex **protein**
 composition and at least one activity based **probe** member of
 combinatorial chemical library, is new.
 DETAILED DESCRIPTION - A composition comprising at least one covalent
 product of a **target protein** member or an
enzyme of a complex **protein** composition and at least one
 activity based **probe** member of combinatorial chemical library
 comprising several members of formula (I) (the members of the library have
 different on rates with the **protein** members):
 R(F-L)-X (I)
 X = a **ligand** present prior to formation of the product or
 added to a reactive functionality to provide the **ligand** having
 the same chemical structure for each of the members of the library;
 L = a bond or linking group, which is the same in each of the members
 of the library;
 F = a **functional group** reactive at an active site
 of a **protein** member and comprising the same reactive
 functionality in each of the members of the library;
 R = a group of less than 1k Dal that is different in each of the
 members of the library.
 R is a part of F or L.
 INDEPENDENT CLAIMS are also included for the following:
 (A) a combinatorial chemical library comprising a number of (I);
 (B) **screening** for members having affinity for an active
protein in a complex mixture of **proteins** from a
 biological source, involves:
 (a) combining with the complex mixture, in an active or inactive
 form, the combinatorial chemical library with active **proteins** to
 form a **conjugate**;
 (b) isolating **conjugates** from the active and inactive
 complex mixture; and
 (c) comparing the **conjugates** formed (the **conjugates**
 in the active mixture absent in the inactive complex mixture are comprised
 only of active **proteins** reactive with the members of the
 combinatorial library);
 (C) **screening** a combinatorial library for members having
 affinity for a **protein** member affecting a cellular phenotype in
 a complex mixture of **proteins** from a natural source involves:
 (a) combining a first truncated combinatorial chemical comprising (I)
 with a first cell type comprising a wild-type **proteome** to react
 the **functional group** with active **proteins** to
 form a **conjugate**;
 (b) determining a change in phenotype of the first cell type;
 (c) combining the combinatorial chemical library having the

ligand with a lysate from the first cell type;

(d) isolating **conjugates** from the wild-type **proteome**; and

(e) characterizing the **protein** in the **conjugate** (the truncated members of the first combinatorial library lack the **ligand**);

(D) a method for identifying a group which has specific affinity for an active site of an **enzyme** involves:

(a) contacting a combinatorial chemical library comprising (I) with a sample containing the **enzyme** to produce an **enzyme conjugate**;

(b) isolating the **enzyme conjugate**; and

(c) degrading the **enzyme conjugate** (the R group that directs the member to the active site is indicative of the R group having an affinity for the active site);

(E) a method of identifying activity-based **probes** having specific affinities for members of a **protein** genus having a common active site involves:

(a) combining candidate activity-based **probes** with at least one active member of the **protein** genus under conditions to form a **conjugate**;

(b) combining candidate activity-based **probes** with the member, inactivated by other than covalent bonding, under the same conditions as with the active member;

(c) isolating any **conjugates** formed with the active member and the inactive member by means of the **ligand** binding to the receptor;

(d) determining the amount of **conjugate** formed with the inactive member and rejecting the candidate activity-based **probes** if the amount of **conjugate** exceeds a predetermined level; and

(e) identifying said probe for an ABP candidate that is not rejected (the activity based probe comprise a functionality specific for the protein genus, a ligand for binding to a bound receptor, a linker and an affinity group and the activity based probe comprises a family of linkers);

(F) a system for identifying activity-based probes for target protein members of a proteome from a combinatorial library of candidate activity-based probes comprising (I), at least one group of related target proteins and a programmed-data processor for receiving and transmitting values (The programmed-data processor comprises a program for evaluating results from the combining of the combinatorial library and the target proteins based on the formation of conjugates of the activity-based probes and the target proteins to determine the affinity of each of the activity-based probes for each of the target proteins. For providing a profile of the affinity of each of the activity-based probes for the target proteins of interests a method is employed which involves combining under binding conditions the activity-based probes and the target proteins such that the activity-based probes binds to the target proteins in relation to the affinity of the activity-based probes to the target proteins. Determining the amount of conjugate of each activity-based probes for each target protein as the results for the data processor, feeding the results to the data processor, and transmitting the values for the binding of each of the activity-based probes to identify activity-based probes forming conjugates); and

(G) a system for identifying activity-based probes from a combinatorial library of candidate compounds comprises a programmed data processor for receiving and transmitting data comprising a program for analyzing the amount of each conjugate and/or the relative abundance of each conjugate and determining the on rates of the probes with the target proteins.

USE - The composition is used for:

(i) analyzing biological fluid, cell fraction or a cell lysate;

(ii) for screening at least one desired biological activity or target

protein;

(iii) screening molecules having affinity for active proteins in a complex mixture of proteins from a biological source;

(iv) for identifying activity-based probes. (all claimed).

ADVANTAGE - The combinatorial library allows for designing drugs for binding to the active site of a target protein. The method easily identifies the biological target molecule for lead compounds, all with varying ability to block cell division. The method shows whether the multiple lead compounds interact with the same or different biological target molecules. The method is simple, takes less time and is economical.

Dwg.0/23

L27 ANSWER 3 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2002-010942 [01] WPIDS
 CR 2002-097342 [68]
 DNN N2002-009086 DNC C2002-002761
 TI **Screening for bioactivity** of candidate compound towards **target proteins** in mixture, useful for generating large number of drug molecules, comprises combining **probe** with mixture and sequestering **proteins conjugated to probe**.
 DC B04 D16 S03 T01
 IN ADAM, G; CRAVATT, B F; LOVATO, M; PATRICELLI, M; SORENSEN, E
 PA (SCRIPPS RES INST
 CYC 94
 PI WO 2001077668 A2 20011018 (200201)* EN 118p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001024349 A 20011023 (200213)
 ADT WO 2001077668 A2 WO 2000-US34167 20001215; AU 2001024349 A AU 2001-24349
 20001215
 FDT AU 2001024349 A Based on WO 200177668
 PRAI US 2000-222532P 20000802; US 2000-195954P 20000410; US 2000-212891P
 20000620
 AB WO 200177668 A UPAB: 20020226
NOVELTY - **Screening** for the **bioactivity** of candidate compound toward a group of related **target proteins** in **proteomic** mixture of **proteins** from cell comprising:
 (a) combining a **probe** with an untreated portion and a portion inactivated with a non-covalent agent;
 (b) sequestering **proteins conjugated with the probe**;
 (c) determining the **proteins** that are sequestered; and
 (d) comparing amount of the **proteins** sequestered, is new.
DETAILED DESCRIPTION - **Screening** (M1) for the **bioactivity** of a candidate compound toward a group of related **target proteins** in a **proteomic** mixture of **proteins** from a cell, by employing at least one **probe** comprising:
 (a) combining at least one **probe** with an untreated portion and with a portion inactivated with a non-covalent agent, of the mixture under conditions for reaction with the **target proteins**
 ;
 (b) sequestering **proteins conjugated with the probe** from each of the mixtures;
 (c) determining the **proteins** that are sequestered; and
 (d) comparing the amount of each of the **proteins** sequestered from the untreated portion and the inactivated portion as indicative of the **bioactivity** of the candidate compound with the

target proteins. The probe comprises a reactive functionality group specific for the group of target proteins and a ligand.

INDEPENDENT CLAIMS are also included for the following:

(1) screening for the bioactivity of a candidate compound toward a group of related target enzymes in a proteomic mixture of proteins from a cell employing at least one probe of formula R asterisk (F-L)-X (I) comprising M1;

(2) determining in a proteomic mixture (A) the presence of active target members (B) comprising a group of related proteins involving:

(a) combining (A) in wild-type form with a probe;
(b) combining (A) after non-specific deactivation with the probe; and

(c) determining the presence of (B) conjugated with the probe in (A) in active and inactive form, where the probe comprises a reactive functionality specific for the active site when active, under conditions for conjugation of the probe to (B) and when the probe conjugated to (B) in (A) in active form and in less amount in inactive form, the presence of (B) is determined;

(3) determining in a plurality of proteomic mixtures the presence of active target members of a group of related proteins which have a common functionality for conjugation at an active site comprising:

(a) combining the mixtures in wild type form with a probe containing a reactive functionality specific for the active site;

(b) determining the presence of target members conjugated with the probe; and

(c) analyzing for the presence of target members conjugated with the probe using simultaneous individual capillary electrokinetic analysis or capillary high performance liquid chromatography (HPLC), where when the target members are conjugated to target members, the presence of active target members is determined;

(4) determining in a proteomic mixture the presence of active target members of a group of related enzymes which have common functionality for conjugation at an active site comprising:

(a) combining the mixture in wild type form with a probe containing a reactive functionality specific for the active site;

(b) combining the mixture after non-specific deactivation with the probe;

(c) determining the presence of target members conjugated with the probe in the proteomic mixtures in active and inactive form, where the probe is conjugated to at least one target member in the mixture in active form and in lesser amount in inactive form, the presence of active members is determined;

(5) a system for identifying active target proteins in a related group of proteins in a sample, using at least one activity-based probe (ABP) binding to several members of the proteins comprising:

(a) a sample containing at least one of the target protein;

(b) ABP of formula R asterisk (Q-L)-X (II); and

(c) a programmed data processor for receiving and transmitting values comprising a program for evaluating results from the combining of ABP and sample resulting in formation of conjugates with active target proteins present to determine the presence of active target proteins and providing a profile of the binding;

(6) a system for determining the status of a biological system in relation to the presence of members of at least one related group of

active proteins, by employing the results from combining (I) and a sample suspected of containing at least one target protein, to produce conjugates of (I) with the target proteins in varying amounts in relation to the amount of each of the active target proteins.

X = a ligand for binding to a reciprocal receptor or a chemically reactive functionality for reacting with a reciprocal functionality for adding a ligand;

L = a linking group, which is the same in each of the members of a library;

Q = a functional group reactive at an active site of a target protein, and is the same reactive functionality in each of the members of the library (preferably a sulfonyl group, fluorophosphonyl or fluorophosphoryl group); and

R asterisk = H or a moiety of less than 1 kDa providing specific affinity for the target protein;

asterisk = intends that R is a part of F or L.

F = functional group reactive at an active site of a target enzyme and is the same reactive functionality in each of the members of the library.

USE - For screening for the bioactivity of a candidate compound towards a group of related target proteins; e.g. for determining the status of a biological system in relation to the presence of the active protein; such as an infectious disease, a response to a therapeutic agent or a response to a candidate drug (claimed). The method is also useful for rapidly generating and developing large numbers of drug candidate molecules or for randomly generating a large number of drug candidates and later optimizing those candidates that show the most medicinal promise; for systematically synthesizing a large number of molecules that may vary greatly in their chemical structure or composition or that may vary in minor aspects of their chemical structure or composition. The screened compounds can be used to indicate the presence of a particular disease in a human or animal, the compounds can stimulate or inhibit the activity of bacteria, viruses, fungi or other infectious agent and/or modulate the effect of a disease by preventing or decreasing the severity of disease or curing a disease such as cancer, diabetes, atherosclerosis, high blood pressure, Parkinson's disease and other disease states.

ADVANTAGE - The method easily identifies the biological target molecule for lead compounds, all with varying ability to block cell division. The method shows whether the multiple lead compounds interact with the same or different biological target molecules. The method is simple, takes less time and is economical.

Dwg.0/24

L27 ANSWER 4 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-582081 [65] WPIDS
 CR 2001-502868 [55]; 2001-557937 [62]; 2001-570624 [57]; 2001-570626 [57];
 2001-570652 [64]
 DNN N2001-433652 DNC C2001-172587
 TI Preparation for diagnosing or treating bipolar affected disorder (BAD) or unipolar depression, or for screening for modulators, comprises a BAD-associated protein isoform.
 DC B04 D16 S03
 IN HERATH, H M A C; PAREKH, R B; ROHLFF, C
 PA (OXFO-N) OXFORD GLYCOSCIENCES UK LTD
 CYC 94
 PI WO 2001063294 A2 20010830 (200165)* EN 163p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TT TZ UA UG US UZ VN YU ZA ZW

ADT AU 2001033957 A 20010903 (200202)
 ADT WO 2001063294 A2 WO 2001-GB791 20010223; AU 2001033957 A AU 2001-33957
 20010223
 FDT AU 2001033957 A Based on WO 200163294
 PRAI US 2000-254830P 20001212; GB 2000-4412 20000224; GB 2000-30050
 20001208
 AB WO 200163294 A UPAB: 20020109
 NOVELTY - A preparation comprising an isolated Bipolar Affected Disorder (BAD)-Associated Protein Isoform (DPIs) which is one of DPI-2-15, 17-25, 29, 30, 34, 35, 37-39, 44, 45, 47, 49-52, 57-60, 65-67, 69, 71-73, 76, 78, 79, 87-90, 92, 93, 96, 103-111, 113, 115, 116, 119-121, 123, 124, 127-129, 135, 139-147, 151, 152, 154, 155, 159-179, 181, or 184-281, is new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) an antibody to one of the DPI's;
 (2) screening, diagnosis or prognosis of BAD or unipolar depression, for determining the stage or severity of BAD or unipolar depression, identifying a subject at risk of developing BAD or unipolar depression, or monitoring the effect of therapy comprising:
 (a) analyzing a test sample of body fluid by two dimensional electrophoresis to generate a two-dimensional array of features where the relative abundance of a chosen feature correlates with the presence, absence, stage or severity of BAD or unipolar depression or predicts the onset or course of BAD or unipolar depression, and comparing the abundance of the chosen feature in the test sample with the abundance in body fluid from persons free from BAD or unipolar depression, or with the abundance of an Expression Reference Feature (ERF) in the test sample; or
 (b) detecting one of the DPI's in a sample of cerebrospinal fluid from the subject;
 (3) kits comprising one of the new preparations, several distinct preparations, an antibody of a preparation or several distinct antibodies of the preparations;
 (4) pharmaceutical compositions comprising the antibody of (1), or a fragment or derivative of (1) containing the binding domain;
 (5) treating or preventing BAD or unipolar depression comprising administering a nucleic acid encoding one of the DPI's or that inhibits the function of one of the DPI's;
 (6) screening for agents that interact with a DPI, a DPI fragment, or a related polypeptide, comprising contacting the DPI, a biologically active portion of a DPI, or a related polypeptide with a candidate agent and determining interaction;
 (7) screening for agents that modulate the expression or activity of a DPI or a DPI-related polypeptide comprising:
 (a) contacting a population of cells expressing a DPI or related polypeptide with a candidate agent;
 (b) contacting a second population of cells expressing the DPI or related polypeptide with a control agent; and
 (c) comparing the level of the DPI or related polypeptide, mRNA encoding them, or the level of induction of a cellular second messenger;
 (8) screening for or identifying agents that modulate the expression or activity of a DPI or related polypeptide comprising:
 (a) administering a candidate agent to a mammal or group of mammals;
 (b) administering a control agent to a second mammal or group of mammals; and
 (c) comparing the level of expression of the DPI or related polypeptide or of mRNA encoding them in the two groups, or comparing the level of induction of a cellular second messenger in the two groups;
 (9) screening for or identifying agents that interact with a DPI or related polypeptide comprising contacting a candidate agent with the DPI or related polypeptide and detecting binding;
 (10) screening for or identifying agents that modulate the activity of a DPI or related polypeptide comprising, in a first aliquot,

contacting a candidate agent with the DPI or related polypeptide and comparing the activity of the DPI or related polypeptide in the first aliquot after addition of the candidate agent with the activity of the DPI or related polypeptide in a control aliquot, or with a previously determined reference range;

(11) screening, diagnosis or prognosis of BAD or unipolar depression or monitoring the effect of an anti-BAD or anti-unipolar depression drug or therapy comprising:

(a) contacting an oligonucleotide **probe** comprising 10 or more consecutive nucleotides complementary to a nucleotide sequence encoding one of the DPI's;

(b) detecting hybridization between the **probe** and the sequence; and

(c) comparing the hybridization with the hybridization in a control sample, or with a previously determined reference range;

(12) screening for agents effective for the treatment of BAD or unipolar depression comprising:

(a) contacting Dkk (dickkopf) with a population of cells expressing the Wnt receptor and **ligand** in the presence of a candidate agent;

(b) contacting Dkk with a second population of cells expressing the receptor and **ligand** in the presence of a control agent;

(c) comparing the binding of the Dkk to the populations of cells, the level of induction of GSK-3 phosphorylation or beta-catenin accumulation in the populations of cells, or the level of a Dkk mediated activity in the cells; and

(d) testing for the ability of agents able to modulate the activity of Dkk to decrease clinical features of BAD in a BAD disease model system; and

(13) screening for agents that modulate the binding of Dkk to a binding partner comprising:

(a) contacting Dkk with the Dkk binding partner in the presence of a candidate or control agent; and

(b) comparing the binding of the Dkk to the binding partner.

ACTIVITY - Antidepressant; antimanic; nootropic; tranquilizer; neuroleptic. No biological data is given.

MECHANISM OF ACTION - Gene therapy.

USE - The DPI's are used to screen, diagnose or prognose of BAD or unipolar depression, determine the stage or severity of BAD or unipolar depression, identify a subject at risk of developing BAD or unipolar depression, or monitor the effect of therapy in a subject. They are also used to screen for or identify agents that interact with a DPI. These agents, antibodies against the DPIS, and nucleic acids encoding the DPIS are used to treat or prevent BAD or unipolar depression (all claimed). Diseases that can be treated are attention deficient disorder, a schizoaffective disorder, a bipolar or a unipolar affective disorder. The DPIS are used in proteomics.

ADVANTAGE - The proteomic approach of using DPIS for screening, diagnosis or prognosis of BAD or unipolar depression overcomes the problems of using gene expression analysis, such as not being able to obtain central nervous system (CNS) tissue from a living patient under normal circumstances.

Dwg.0/3

L27 ANSWER 5 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-476115 [51] WPIDS
 DNC C2001-142814
 TI New lipid metabolism **enzymes** and the polynucleotides encoding them, useful in diagnosing, treating, and preventing cancer, neurological, autoimmune, inflammatory, gastrointestinal or cardiovascular disorders.
 DC B04 C06 D16
 IN AZIMZAI, Y; BAUGHN, M R; GANDHI, A R; HILLMAN, J L; LU, D A M; NGUYEN, D B; TANG, Y T; WALIA, N K; YUE, H

PA (INCY-N) INCYTE GENOMICS INC
 CYC 94
 PI WO 2001053468 A2 20010726 (200151)* EN 120p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001031053 A 20010731 (200171)
 ADT WO 2001053468 A2 WO 2001-US2060 20010118; AU 2001031053 A AU 2001-31053
 20010118
 FDT AU 2001031053 A Based on WO 200153468
 PRAI US 2000-183683P 20000217; US 2000-177732P 20000121; US 2000-178885P
 20000128; US 2000-181863P 20000211
 AB WO 200153468 A UPAB: 20010910
 NOVELTY - A new isolated polypeptide comprises an amino acid sequence comprising:
 (a) 338, 370, 282, 736, 789, 393, 421, 152, 682 or 330 amino acids fully defined in the specification;
 (b) a naturally occurring amino acid sequence having at least 90% sequence identity to (a);
 (c) a **biologically active** fragment of (a); and
 (d) an immunogenic fragment of (a).
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) an isolated polynucleotide comprising:
 (a) an isolated polynucleotide encoding the polypeptide;
 (b) a recombinant polynucleotide having a promoter sequence operably linked to (1a);
 (c) a polynucleotide sequence having 2195, 3395, 1560, 2860, 3544, 2776, 3176, 459, 2756 or 1672 bp fully defined in the specification;
 (d) a naturally occurring polynucleotide sequence having at least 90% sequence identity to (c);
 (e) a polynucleotide sequence complementary to (c) or (d);
 (f) an RNA equivalent of (c)-(e); or
 (g) at least 60 contiguous nucleotides of (c), (d), (e) or (f);
 (2) a cell transformed with the recombinant polynucleotide;
 (3) a transgenic organism comprising the recombinant polynucleotide;
 (4) a method for producing the polypeptide;
 (5) an isolated antibody, which specifically binds to the polypeptide;
 (6) methods for detecting a target polynucleotide in a sample;
 (7) a method (M1) for **screening** a compound for effectiveness as an agonist of the polypeptide comprising:
 (a) exposing a sample comprising the polypeptide to a compound; and
 (b) detecting agonist activity in the sample;
 (8) a method (M2) for **screening** a compound for effectiveness as an antagonist of the polypeptide comprising:
 (a) exposing the sample comprising the polypeptide to a compound; and
 (b) detecting antagonist activity in the sample;
 (9) compositions comprising:
 (a) the polypeptide and a pharmaceutical excipient;
 (b) agonist compound identified by the method and a pharmaceutical excipient; or
 (c) antagonist compound identified by the method and a pharmaceutical excipient;
 (10) methods (M3) for treating a disease or condition associated with decreased expression of functional lipid metabolism **enzymes** (LME) comprising administering to a patient the composition of (9a) or (9b);
 (11) a method (M4) for treating a disease or condition associated with overexpression of functional LME comprising administering to the

patient the composition of (c);

(12) a method (M5) of screening for a compound that specifically binds to the polypeptide comprising:

(a) combining the polypeptide with at least one test compound; and

(b) detecting binding of the polypeptide to the test compound, thus identifying a compound that specifically binds to the polypeptide;

(13) a method (M6) of screening for a compound that modulates the activity of the polypeptide comprising:

(a) combining the polypeptide with at least one test compound under conditions permissive for the activity of the polypeptide;

(b) assessing the activity of the polypeptide in the presence of the test compound; and

(c) comparing the activity of the polypeptide in the presence of the test compound with the activity of the polypeptide in the absence of the test compound, where a change in the activity of the polypeptide in the presence of the test compound is indicative of a compound that modulates the activity of the polypeptide;

(14) a method (M7) for screening a compound for effectiveness in altering expression of a target polynucleotide, where the target polynucleotide comprises the sequence cited above, comprising:

(a) exposing a sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide;

(b) detecting altered expression of the target polynucleotide; and

(c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound; and

(15) a method (M8) for assessing toxicity of a test compound comprising:

(a) treating a biological sample containing nucleic acids with the test compound;

(b) hybridizing the nucleic acids of the treated biological sample with a probe comprising at least 20 contiguous nucleotides of the polynucleotide, where a specific hybridization complex is formed between the probe and a target polynucleotide in the biological sample, the target polynucleotide comprising the polynucleotide sequence cited above or its fragment;

(c) quantifying the amount of hybridization complex; and

(d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, where a difference in the amount of hybridization complex in the treated biological sample is indicative of toxicity of the test compound.

ACTIVITY - Cytostatic; immunosuppressive; anti-inflammatory; cardiovascular; cerebroprotective; neuroprotective; antibacterial; fungicide; virucide; antiparasitic.

No details of clinical tests given.

MECHANISM OF ACTION - Gene therapy.

USE - The proteins and nucleic acids encoding the enzymes are useful in diagnosing, treating, and preventing cancer, neurological, autoimmune, inflammatory, gastrointestinal, and cardiovascular disorders, and in assessing the effects of exogenous compounds on the expression of nucleic acid and amino acid sequences of lipid metabolism enzymes (LME). LME may also be used to treat or prevent a disorder associated with decreased expression or activity of LME, such as tumors or cancers (e.g. adenocarcinoma, leukemia, lymphoma), motor neuron disorders, multiple sclerosis and other demyelinating diseases, developmental disorders of the central nervous system, bacterial, viral, fungal and parasitic diseases. LME may further be used to screen for compounds that specifically bind to or modulate the activity of LME, and to produce antibodies.

Polynucleotides encoding LME are useful for somatic and germline gene therapy, to detect and quantify gene expression in biopsied tissues in which expression of LME may be correlated with disease, to detect the

presence of associated disorders, to analyze the proteome of a tissue or cell type, to generate hybridization probes, and to screen libraries of compounds in various drug screening techniques. Antibodies which specifically bind LME may be used for the diagnosis of disorders characterized by expression of LME, in assays to monitor patients being treated with LME or its antagonists, agonists or inhibitors, or to detect the presence of any peptide which shares one or more antigenic determinants with LME.

Dwg. 0/0

L27 ANSWER 6 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
AN 2001-451868 [48] WPIDS
CR 2001-061976 [07]; 2001-656926 [66]
DNC C2001-136537
TI Detecting a nucleic acid useful in e.g. diagnosing genetic, bacterial or viral diseases, by contacting the nucleic acid with oligonucleotides attached to nanoparticles and having sequences complementary a portion of the nucleic acid.
DC B04 D16
IN ELGHANIAN, R; LETSINGER, R L; LI, Z; MIRKIN, C A; MUCIC, R C; STORHOFF, J J; TATON, T A
PA (NANO-N) NANOSPHERE INC
CYC 93
PI WO 2001051665 A2 20010719 (200148)* EN 229p
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2001032795 A 20010724 (200166)
ADT WO 2001051665 A2 WO 2001-US1190 20010112; AU 2001032795 A AU 2001-32795
20010112
FDT AU 2001032795 A Based on WO 200151665
PRAI US 2001-760500 20010112; US 2000-176409P 20000113; US 2000-200161P
20000426; US 2000-603830 20000626
AB WO 200151665 A UPAB: 20011227
NOVELTY - Detecting a nucleic acid having at least 2 portions, comprises contacting the nucleic acid with one or more types of nanoparticles having oligonucleotides attached to the nanoparticles and having sequences complementary to portions of the sequence of the nucleic acid.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) methods of detecting a nucleic acid having at least 2 portions comprising:
(a) contacting the nucleic acid with one or more types of nanoparticles having oligonucleotides attached to the nanoparticles and having sequences complementary to portions of the sequence of the nucleic acid, under conditions allowing the hybridization of the oligonucleotides on the nanoparticles with the nucleic acid; and
(b) observing a detectable change brought about by hybridization of the oligonucleotides on the nanoparticles with the nucleic acid;
(2) kits comprising at least one container holding a composition containing at least 2 types of nanoparticles having oligonucleotides attached to it, where the first type has a sequence complementary to the sequence of a first portion of a nucleic acid, and the oligonucleotides on the second type of nanoparticles has a sequence complementary to the sequence of a second portion of the nucleic acid;
(3) an aggregate probe comprising at least 2 types of nanoparticles having oligonucleotides attached to it, the nanoparticles of the aggregate probe are bound to each other as a result of the hybridization of some of the oligonucleotides attached to them, and at least one of the nanoparticles of the aggregate probe having

oligonucleotides attached to it which have a hydrophobic group on the end not attached to the nanoparticles;

(4) a kit comprising a container holding a core **probe** having at least 2 types of nanoparticles having oligonucleotides attached to it and the nanoparticles of the core **probe** is bound to each other as a result of the hybridization of some of the oligonucleotides attached to them;

(5) a core **probe** comprising at least 2 types of nanoparticles having oligonucleotides attached to it;

(6) a substrate having nanoparticles attached to it;

(7) a metallic or semiconductor nanoparticle having oligonucleotides attached to it which are labeled with fluorescent molecule at the end not attached to the nanoparticle;

(8) a satellite **probe** comprising a particle having attached oligonucleotides, and **probe** oligonucleotides hybridized to the oligonucleotides attached to the nanoparticles;

(9) methods of nanofabrication;

(10) nanomaterials or nanostructures composed of nanoparticles having oligonucleotides attached to it and being held by oligonucleotide connectors;

(11) a composition comprising at least 2 types of nanoparticles having oligonucleotides attached to it;

(12) an assembly of containers holding nanoparticles having oligonucleotides attached to them;

(13) a nanoparticle having multiple oligonucleotides attached to it;

(14) a method of separating a selected nucleic acid having at least 2 portions from other nucleic acid;

(15) methods of binding oligonucleotides to charged nanoparticles to produce stable nanoparticle-oligonucleotide conjugates;

(16) nanoparticle-oligonucleotide conjugates which are nanoparticles having oligonucleotides attached to them, where the oligonucleotides are present on the surface of the nanoparticles at a surface density sufficient so that the conjugates are stable, and at least some of the oligonucleotides have sequences complementary to at least one portion of the nucleic acid or oligonucleotide sequence;

(17) nanoparticles having oligonucleotides attached to them which comprises at least one type of recognition oligonucleotides having a sequence complementary to a portion of the nucleic acid sequence, and a type of diluent oligonucleotides; and

(18) methods of detecting a nucleic acid.

USE - The methods are useful for detecting nucleic acids, natural or synthetic, and modified or unmodified. The methods may also be applied in the diagnosis of genetic, bacterial and viral diseases, in forensics, in DNA sequencing, for paternity testing, for cell line authentication, and for monitoring gene therapy. The methods are further useful in research and analytical laboratories in DNA sequencing, in the field to detect the presence of specific pathogens, for quick identification of an infection to assist in drug prescription, and in homes and health centers for inexpensive first-line screening.

ADVANTAGE - The methods, which are based on observing color change with the naked eye, are cheap, fast, simple, robust (reagents are stable), do not require specialized or expensive equipment, and little or no instrumentation is required.

Dwg.0/46

L27 ANSWER 7 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-441281 [47] WPIDS
 DNN N2001-326466 DNC C2001-133212
 TI Composite nanospheres, useful as carriers for diagnostic or therapeutic agents, comprise fluid core containing inorganic nanoparticles and shell of hydrophilic polymer.
 DC A13 A14 A82 A96 A97 B04 B07 D16 E19 G02 J04 P41 S03
 IN BIBETTE, J; BOSC, E; ELAISSARI, A; MANDRAND, B; MONDAIN, M O; PICHOT, C

PA (INMR) BIO MERIEUX; (CNRS) CNRS CENT NAT RECH SCI; (CNRS) CENT NAT RECH
 SCI; (MOND-I) MONDAIN-MONVAL O
 CYC 94
 PI WO 2001033223 A1 20010510 (200147)* FR 28p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 FR 2800635 A1 20010511 (200147)
 AU 2001012882 A 20010514 (200149)
 ADT WO 2001033223 A1 WO 2000-FR3085 20001106; FR 2800635 A1 FR 1999-14194
 19991105; AU 2001012882 A AU 2001-12882 20001106
 FDT AU 2001012882 A Based on WO 200133223
 PRAI FR 1999-14194 19991105
 AB WO 200133223 A UPAB: 20010822
 NOVELTY - Composite nanospheres (A):
 (i) have diameter 50-1000, best 100-200, nm, plus or minus 5%;
 (ii) have a liquid core of organic phase containing inorganic
 nanoparticles (NP) distributed in it; and
 (iii) has an envelope comprising at least one hydrophilic polymer (B)
 prepared from a water-soluble monomer, especially an N-alkyl or
 N,N-dialkyl acrylamide.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:
 (1) conjugate (C1) of (A), having reactive
 functional groups on the surface, linked to at least one
 ligand, i.e. antibody (or fragment), protein,
 polypeptide, enzyme, polynucleotide, probe, primer,
 nucleic acid fragment and biotin;
 (2) reagent (R) containing (A) or C1;
 (3) diagnostic composition containing (R);
 (4) conjugate (C2) of (A) coupled to at least one
 ligand, i.e. a pharmaceutical compound, antisense probe,
 gene repair agent, therapeutic gene or agent that blocks/inhibits
 protein activity;
 (5) therapeutic or prophylactic composition containing C2;
 (6) conjugate (C3) of (A) coupled to at least one
 ligand, i.e. a cage molecule, chelating agent or catalyst.
 USE - (A) are used as carriers for a wide variety of active compounds
 (ligands), e.g. for use in diagnostic, therapeutic, prophylactic
 or cosmetic materials, also in paints, inks, plastics or as catalysts.
 Typical applications are as carriers of nucleic acid or proteins
 ; as reagents in immunological or nucleic acid binding tests (for
 detecting or quantifying antigens, antibodies or other proteins
), and in gene therapy.
 ADVANTAGE - The use of a liquid core allows separation of the
 particles even in a weak magnetic field.
 Dwg.0/0

L27 ANSWER 8 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-425161 [45] WPIDS
 DNN N2001-315437 DNC C2001-128597
 TI Composite particles, useful as carriers for diagnostic or therapeutic
 agents, comprise matrix of hydrophobic polymer, containing stabilized and
 dispersed inorganic nanoparticles.
 DC A13 A14 A96 A97 B04 B07 D16 E19 J04 P41 S03
 IN BIBETTE, J; BOSC, E; ELAISSARI, A; MANDRAND, B; MONDAIN, M O; PICHOT, C;
 MONDAIN-MONVAL, O
 PA (INMR) BIO MERIEUX; (CNRS) CNRS CENT NAT RECH SCI; (CNRS) CENT NAT RECH
 SCI; (PICH-I) PICHOT C
 CYC 94

PI WO 2001033224 A1 20010510 (200145)* FR 33p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

FR 2800636 A1 20010511 (200145)

AU 2001012883 A 20010514 (200149)

ADT WO 2001033224 A1 WO 2000-FR3086 20001106; FR 2800636 A1 FR 1999-14195
 19991105; AU 2001012883 A AU 2001-12883 20001106

FDT AU 2001012883 A Based on WO 200133224

PRAI FR 1999-14195 19991105

AB WO 200133224 A UPAB: 20010813

NOVELTY - Composite particle (CP) has diameter 50-1000 nm, (preferably 100-250 nm) and consists of:

(i) a matrix of hydrophobic polymer; and
 (ii) inorganic nanoparticles, stabilized and dispersed, reactively homogeneously, within the matrix.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing CP;
 (2) conjugate (C1) of CP, having reactive functional groups on the surface, linked to at least one ligand, such as antibody (or fragment), protein, polypeptide, enzyme, polynucleotide, probe, primer, nucleic acid fragment and biotin;

(3) reagent (R) containing at least one C1;
 (4) diagnostic composition containing (R);
 (5) conjugate (C2) of CP coupled to at least one ligand, such as a pharmaceutical compound, antisense probe, gene repair agent, therapeutic gene or agent that blocks/inhibits protein activity; and

(6) conjugate (C3), having reactive functional groups on its surface, coupled to at least one ligand, including a cage molecule, chelating agent or catalyst.

USE - CP are used as carriers for a wide variety of active compounds (ligands), such as for use in diagnostic, therapeutic or prophylactic materials, also as catalysts. Typical applications are as carriers of nucleic acid or proteins; as reagents in immunological or nucleic acid binding tests (for detecting or quantifying antigens, antibodies or other proteins), and in gene therapy.

ADVANTAGE - Compared with conventional magnetic particles, CP have greater specific surface area and are less subject to sedimentation.

Dwg. 0/0

L27 ANSWER 9 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2001-418080 [44] WPIDS

DNN N2001-309733 DNC C2001-126433

TI Novel human protease proteins (PRTS) useful for diagnosing, treating, preventing gastrointestinal, cardiovascular, autoimmune/inflammatory, cell proliferative disorders associated with abnormal expression of PRTS.

DC B04 D16 P14 S03

IN AU-YOUNG, J; BAUGHN, M R; BURFORD, N; LAL, P; LU, D A M; NGUYEN, D B; REDDY, R; TANG, Y T; YANG, J; YAO, M G; YUE, H

PA (INCY-N) INCYTE GENOMICS INC

CYC 94

PI WO 2001046443 A2 20010628 (200144)* EN 129p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC

LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001022857 A 20010703 (200164)

ADT WO 2001046443 A2 WO 2000-US34811 20001219; AU 2001022857 A AU 2001-22857
20001219

FDT AU 2001022857 A Based on WO 200146443

PRAI US 2000-179903P 20000202; US 1999-172055P 19991223; US 2000-177334P
20000121; US 2000-178884P 20000128

AB WO 200146443 A UPAB: 20010809

NOVELTY - Isolated human protease proteins (I) (referred as PRTS 1-14) having fully defined sequence (PS) of 1055, 358, 467, 187, 289, 960, 525, 795, 919, 209, 77, 414, 397 or 145 (S1-S14) amino acids as given in specification, a naturally occurring amino acid sequence having 90% sequence identity to PS, or biologically active or immunogenic fragment of PS, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide (II) encoding (I);
- (2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);
- (3) a cell (IV) transformed with (III);
- (4) a transgenic organism comprising (III);
- (5) preparation of (I);
- (6) an isolated antibody that specifically binds to (I);
- (7) an isolated polynucleotide (N1) comprising a sequence selected from:
 - (a) a polynucleotide sequence selected from a fully defined sequence of 4028, 1422, 1911, 854, 1386, 3323, 2123, 2893, 4170, 767, 1538, 1497, 1194 (S15-S27) or 438 (S28) nucleotides as given in the specification;
 - (b) a naturally occurring polynucleotide sequence having at least 90% sequence identity to a polynucleotide selected from S15-S28;
 - (c) a polynucleotide sequence complementary to the sequence of (a) or (b);
 - (d) an RNA equivalent of (a) to (c);
 - (8) an isolated polynucleotide comprising 60 contiguous nucleotides of N1;
- (9) detecting a target polynucleotide in a sample which comprises a sequence of N1 involves:
 - (a) hybridizing the sample with a probe comprising at least 20 contiguous nucleotides which is complementary to the target polynucleotide in the sample and which specifically hybridizes to the target polynucleotide, under conditions, by which a hybridization complex is formed between the probe and the target polynucleotide or its fragments, and then detecting the presence or absence of the hybridization complex, and, optionally, if present the amount of the target polynucleotide is also quantitated; or
 - (b) amplifying the target polynucleotide or its fragments by polymerase chain reaction (PCR) and then detecting the presence or absence of the amplified target polynucleotide or its fragment optionally, if present the amount of the target polynucleotide is also quantitated;
- (10) screening a compound for effectiveness as an agonist or antagonist of (I) involves exposing a sample comprising (I) to a compound and detecting agonist or antagonist activity in the sample;
- (11) screening for a compound that specifically binds to (I) involves combining (I) with a test compound under suitable conditions and then detecting binding of (I) to the test compound, thus identifying a compound that specifically binds to (I);

(12) screening for a compound that modulates the activity of (I) involves combining (I) with a test compound under conditions permissive for the activity of (I), assessing the activity of (I) in the presence of the test compound and then comparing the activity of (I) in the presence of test compound with the activity of (I) in the absence of the test compound, where a change in the activity of (I) in the presence

of the test compound is indicative of a compound that modulates the activity of (I);

(13) screening a compound for effectiveness in altering expression of a target polynucleotide which comprises a sequence of (S15)-(S27) or (S28) involves exposing the sample comprising the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide and comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound; and

(14) a method for assessing toxicity of a test compound, comprising:

(a) treating a biological sample containing nucleic acids with the test compound;

(b) hybridizing the nucleic acids of the sample with a **probe** comprising at least 20 contiguous nucleotides of N1 under conditions where a specific hybridization complex is formed between the **probe** and target polynucleotide, where the target polynucleotide comprises a sequence of N1 or its fragment;

(c) quantifying the amount of hybridization complex;

(d) comparing the amount of complex in the treated sample with the amount of complex in an untreated sample, where a difference in the amounts is indicative of toxicity of the test compound.

ACTIVITY - Antiinflammatory; cytostatic; antiatherosclerotic; hypotensive; antitumor; cardiant; anti-HIV; immunosuppressive; dermatological; neuroprotective; antiviral; nootropic; antibacterial; antiinfertility. No supporting biological data is given.

MECHANISM OF ACTION - PRTS expression or activity modulators; gene therapy.

No supporting biological data is given.

USE - The pharmaceutical compositions comprising (I) or an agonist of (I) is useful for treating a disease or condition associated with decreased expression of functional PRTS. The pharmaceutical composition comprising the antagonist of (I) is useful for treating a disease or condition associated with overexpression of (I). (I) is useful for identifying compounds that bind to (I) or which modulate activity of (I).

(I) and (II) are useful for diagnosing, treating or preventing a gastrointestinal disorder such as anorexia, cardiovascular disorder such as atherosclerosis and hypertension, autoimmune/inflammatory disorders such as acquired immuno deficiency syndrome (AIDS), cell proliferative disorders such as actinic keratosis, a developmental disorders such as epilepsy, an epithelial disorders such as allergic contact dermatitis, neurological disorders such as Alzheimer's disease, and reproductive disorders such as infertility.

(II) is useful for creating knock out or knock in humanized animals or transgenic animals to model human disease. (II) is useful for somatic or germline gene therapy for treating the above mentioned disorders. (II) is also useful for developing genetic linkage maps, detecting differences in chromosomal location due to translocation, inversion etc.

(I), its catalytic or immunogenic fragments are useful for screening libraries of compounds in several drug screening assays. (I) is useful for analyzing the proteome of a tissue or cell type.

Antibodies which bind to (I) may be used for diagnosis of disorders characterized by expression of (I) or in assays to monitor patients being treated with PRTS or agonists, antagonists or inhibitors of PRTS. The antibodies specific for PRTS, or PRTS or its fragments may be used as elements on a microarray which is useful to monitor protein-protein interaction, drug-target interaction, etc. The antibodies are also useful for assessing toxicity of a test compound. The method involves treating biological sample containing protein with the test compound and incubating with antibodies specific to the PRTS polypeptides.

Dwg.0/0

DNC C2001-118895
 TI Novel human lyase proteins (HLYAP) useful for diagnosing, treating and preventing neurological, reproductive, cell proliferative and inflammatory disorders associated with abnormal expression of HLYAP.
 DC B04 D16
 IN BANDMAN, O; BAUGHN, M R; HILLMAN, J L; LU, D A M; TANG, Y T; YUE, H
 PA (INCY-N) INCYTE GENOMICS INC
 CYC 94
 PI WO 2001044445 A2 20010621 (200141)* EN 102p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TR TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2001024309 A 20010625 (200162)
 ADT WO 2001044445 A2 WO 2000-US33815 20001213; AU 2001024309 A AU 2001-24309
 20001213
 FDT AU 2001024309 A Based on WO 200144445
 PRAI US 1999-172307P 19991216
 AB WO 200144445 A UPAB: 20010724
 NOVELTY - Isolated human lyase proteins (I) (referred as HLYAP 1-10) having defined sequence (PS) of 243, 425, 216, 343, 74, 176, 374, 780, 594 or 298 amino acids given in specification, a naturally occurring amino acid sequence having 90% sequence identity to PS, or biologically active or immunogenic fragment of PS, is new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) isolated polynucleotide (II) encoding (I). (II) comprises a defined sequence of 1686, 2053, 2490, 1230, 955, 849, 1919, 2735, 2822 (S11-S19) or 1774 (S20) nucleotides given in the specification, is a naturally occurring polynucleotide sequence having 90% identity to the above mentioned polynucleotide sequences, a polynucleotide sequence which is complementary to the above mentioned sequences, or is a RNA equivalent of the above mentioned sequences;
 (2) recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);
 (3) cell (IV) transformed with (III);
 (4) transgenic organism comprising (III);
 (5) preparation of (I);
 (6) isolated antibody that specifically binds to (I);
 (7) detecting a target polynucleotide in a sample which comprises a sequence of (II) comprising hybridizing the sample with a probe containing at least 20 contiguous nucleotides which is complementary to the target polynucleotide in the sample and which specifically hybridizes to the target polynucleotide, under conditions, by which a hybridization complex is formed between the probe and the target polynucleotide or its fragments, and then detecting the presence or absence of the hybridization complex, and, optionally, if present the amount of the target polynucleotide is also quantitated. Alternately, the method is carried out by amplifying the target polynucleotide or its fragments by polymerase chain reaction (PCR) and then detecting the presence or absence of the target polynucleotide or its fragment;
 (8) isolated polynucleotide comprising 60 contiguous nucleotides of (II);
 (9) screening a compound for effectiveness as an agonist or antagonist of (I) comprising exposing a sample containing (I) to a compound and detecting agonist or antagonist activity in the sample;
 (10) screening for a compound that specifically binds to (I) comprising combining (I) with a test compound under suitable conditions and then detecting binding of (I) to the test compound, thus identifying a compound that specifically binds to (I);

(11) **screening** for a compound that modulates the activity of (I) comprising combining (I) with a test compound under conditions permissive for the activity of (I), assessing the activity of (I) in the presence of the test compound and then comparing the activity of (I) in the presence of test compound with the activity of (I) in the absence of the test compound. A change in the activity of (I) in the presence of the test compound is indicative of a compound that modulates the activity of (I); and

(12) **screening** a compound for effectiveness in altering expression of a target polynucleotide which comprises a sequence of (S11)-(S19) or (S20) comprising exposing the sample containing the target polynucleotide to a compound, under conditions suitable for the expression of the target polynucleotide and comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound.

ACTIVITY - Antiarteriosclerotic; antiatherosclerotic; antiinflammatory; antipsoriatic; cytostatic; hepatotrophic; immunosuppressive; antiinfertility; gynecological; osteopathic; anticonvulsant; cerebroprotective; nootropic; neuroprotective; antiparkinsonian; tranquilizer; neuroleptic; anti-HIV; dermatological; antiallergic; antianemic; antiasthmatic; nephrotrophic; antigout; antiarthritic; antirheumatic; antiulcer; ophthalmological. No supporting data is given.

MECHANISM OF ACTION - Gene therapy.

USE - (I) is useful for identifying compounds that bind to (I) or which modulate activity of (I). (II) is useful for assessing toxicity of a test compound.

(I) and (II) are useful for diagnosing, treating or preventing cell proliferative disorders such as actinic keratosis, arteriosclerosis, atherosclerosis, bursitis, cirrhosis, hepatitis, psoriasis, mixed connective tissue disease (MCTD), myelofibrosis, a cancer such as adenocarcinoma, leukemia, lymphoma or melanoma; reproductive disorders such as infertility, ovulatory defects, disruption of the estrous cycle, disruptions of the menstrual cycle, endometrial and ovarian tumors, ectopic pregnancies and teratogenesis; neurological disorders such as epilepsy, stroke, Alzheimer's disease, Huntington's disease, Parkinson's disease, bacterial and viral meningitis, brain abscess, Creutzfeldt-Jakob disease, cerebral palsy, autonomic nervous system disorders, cranial nerve disorders, spinal cord diseases, muscular dystrophy and other neuromuscular disorders, peripheral nervous system disorders, anxiety, amnesia, and schizophrenic disorders; inflammatory disorders such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, allergies, amyloidosis, anemia, asthma, autoimmune hemolytic anemia, autoimmune thyroiditis, autoimmune polyendocrinopathy and Crohn's disease, atopic dermatitis, Goodpasture's syndrome, gout, multiple sclerosis, osteoarthritis, osteoporosis, psoriasis, rheumatoid arthritis or ulcerative colitis and uveitis.

(II) is useful to detect upstream sequences such as promoters and regulatory elements. (II) is useful for creating knock out or knock in humanized animals or transgenic animals to model human disease. (II) is useful for somatic or germline gene therapy for treating the above disorders. Oligonucleotide primers derived from (II) may be used to detect single nucleotide polymorphisms. (II) may be used for generating hybridization **probes** useful in mapping the naturally occurring genomic sequences. (II) is useful for developing genetic linkage maps, detecting differences in chromosomal location due to translocation or inversion. Oligonucleotides or longer fragments derived from any of the polynucleotide sequences may be used as elements on a microarray. (I), its catalytic or immunogenic fragments are useful for **screening** libraries of compounds in several drug **screening** assays. (I) is useful for analyzing the **proteome** of a tissue or cell type. A vector encoding (I) or its fragments is useful for treating the above mentioned disorders. Antibodies which bind to (I) may be used for

diagnosis of disorders characterized by expression of (I) or in assays to monitor patients being treated with HLYAP or agonists, antagonists or inhibitors of HLYAP. The antibodies specific for HLYAP may be used as elements on a microarray which is useful to monitor protein interaction and drug-target interaction. The antibodies are also useful for assessing toxicity of a test compound.

Dwg.0/0

L27 ANSWER 11 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-380124 [40] WPIDS
 DNC C2001-116357
 TI New biotinylated electrically conductive copolymers useful for producing biosensors or biochips bearing arrays of probes.
 DC A23 A89 B04 D16
 IN COSNIER, S
 PA (BIOP-N) BIOPIXEL LTD
 CYC 1
 PI US 6197881 B1 20010306 (200140)* 22p
 ADT US 6197881 B1 US 1999-376692 19990818
 PRAI US 1999-376692 19990818
 AB US 6197881 B UPAB: 20010719
 NOVELTY - Biotinylated electrically conductive copolymers (I) are new.
 DETAILED DESCRIPTION - Electrically conductive copolymers of formula (I) are new:
 A, B' = monomer units;
 w', y = 0 or more;
 x, z = 1 or more;
 L1, L2 = covalent linkers or spacer arms;
 L3 = a functional group; and
 Bt = covalently bonded biotin, optionally complexed with avidin, streptavidin or their derivatives.

An INDEPENDENT CLAIM is also included for the production of (I) by electrochemical or chemical copolymerization of A-L1-(L2-Bt)_z with B-(L3)_{w'} on a support.

USE - Biosensors or biochips can be produced by forming a layer of (I) on a support, e.g. a metal electrode, by electrochemical or chemical polymerization, reacting the biotin groups with avidin, optionally forming multiple layers by sequential biotin-avidin coupling, and reacting the outermost biotin or avidin groups with avidin or biotin conjugates of ligands that can function as probes, especially proteins, peptides, polypeptides, lectins, antibodies, receptors, enzymes, single-domain antibodies, monoclonal catalytic antibodies, immunoadhesins, sugars, oligosaccharides, DNA, cDNA or RNA sequences, oligonucleotides, peptide nucleic acids, lipids, phospholipids, fluorescent probes, spin labels, metal complexes, polymers or monomers.

Dwg.0/12

L27 ANSWER 12 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-258140 [26] WPIDS
 DNC C2001-077861
 TI Replicable genetic packages displaying compounds or including nucleic acid tags that serve to record a characteristic of a compound, useful for screening large libraries of compounds to identify compounds with a desired activity.
 DC B04 D16
 IN BARRETT, R W; CWIRLA, S E; DOWER, W J; GALLOP, M; WOIWODE, T F
 PA (BARR-I) BARRETT R W; (DOWE-I) DOWER W J; (GALL-I) GALLOP M; (XENO-N)
 XENOPORT INC
 CYC 94
 PI WO 2001023619 A1 20010405 (200126)* EN 130p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000078397 A 20010430 (200142)
 ADT WO 2001023619 A1 WO 2000-US26849 20000929; AU 2000078397 A AU 2000-78397
 20000929

FDT AU 2000078397 A Based on WO 200123619

PRAI US 1999-156675P 19990929

AB WO 200123619 A UPAB: 20010515

NOVELTY - Replicable genetic packages that display various compounds are new. The replicable genetic packages include compounds attached to it, or nucleic acid tags that may serve to record a characteristic of the compound.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also provided for the following:

(1) a replicable genetic package (R1) displaying a compound other than an expressed polypeptide, where the replicable genetic package comprises a heterologous nucleic acid tag encoding a characteristic of the compound;

(2) a replicable genetic package (R2) displaying a compound other than an expressed polypeptide, where the replicable genetic package and the compound are attached via a linker;

(3) a replicable genetic package (R3) displaying a compound, where the replicable genetic package comprises a heterologous nucleic acid tag encoding a characteristic of the compound by a code other than the standard genetic code;

(4) a method (M1) of **screening** a library of compounds, comprising providing replicable genetic packages displaying different compounds, where the compounds are other than an expressed polypeptide; and assaying the replicable genetic packages to identify at least one replicable genetic package displaying at least one compound with a desired property;

(5) a method (M2) of **screening** a library of compounds, comprising:

(a) providing different replicable genetic packages each displaying a compound other than an expressed polypeptide, and harboring different heterologous nucleic acid tags;

(b) assaying the replicable genetic packages to identify at least one replicable genetic package displaying at least one compound with a desired property; and

(c) decoding the heterologous nucleic acid tag of at least one replicable genetic package to identify a characteristic of the compound with the desirable property; and

(6) another method of **screening** a library of compounds, comprising:

(a) for each compound to be **screened**, contacting the compound with a replicable genetic package to form replicable genetic packages displaying different compounds, where different replicable genetic packages harbor different heterologous nucleic acid tags; and

(b) decoding the heterologous nucleic acid tag of at least one replicable genetic package to identify a characteristic of at least one compound with the desirable property.

USE - The replicable genetic packages can be used to rapidly **screen** large libraries of compounds to identify compounds having a desired activity, for e.g. they can be used to identify library members capable of:

- (a) binding to a receptor;
- (b) being transported into or through a cell;
- (c) functioning as a substrate or inhibitor of an **enzyme**;
- (d) killing bacteria, fungi or other microorganisms;
- (e) triggering signal transduction; and
- (f) agonizing or antagonizing a receptor.

ADVANTAGE - The use of compound-bearing replicable genetic packages allows for ease of quantification and high sensitivity in a variety of different types of assays.

Dwg.0/22

L27 ANSWER 13 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-244811 [25] WPIDS
 DNN N2001-174296 DNC C2001-073482
 TI Novel human **protein** phosphatase and kinase **proteins**
 for diagnosis, treatment and prevention of gastrointestinal, immune system, neurological and cell proliferative disorders.
 DC B04 D16 P14 S03
 IN AZIMZAI, Y; BANDMAN, O; BAUGHN, M R; HILLMAN, J L; LU, D A M; TANG, Y T;
 YUE, H
 PA (INCY-N) INCYTE GENOMICS INC
 CYC 94
 PI WO 2001020004 A2 20010322 (200125)* EN 103p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000078297 A 20010417 (200140)
 ADT WO 2001020004 A2 WO 2000-US25515 20000914; AU 2000078297 A AU 2000-78297
 20000914
 FDT AU 2000078297 A Based on WO 200120004
 PRAI US 1999-154141P 19990915
 AB WO 200120004 A UPAB: 20011129
 NOVELTY - An isolated human **protein** phosphatase and kinase **proteins** (PPHKP) (I) comprising a 329, 141, 447, 666, 358, 470, 150, 253, 442, 659 or 145 residue amino acid sequence (S1), fully defined in the specification, a naturally occurrence sequence having at least 90 % identity to S1, and **biologically active** and **immunogenic** fragments of S1, is new.
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

- (1) an isolated polynucleotide (II) encoding (I);
- (2) a recombinant polynucleotide (III) comprising a promoter sequence operably linked to (II);
- (3) a cell (IV) transformed with (III);
- (4) a transgenic organism (V) comprising (III);
- (5) production of (I), comprising culturing (IV) under expression conditions, and recovering the polypeptide;
- (6) an isolated antibody (VI) which specifically binds to (I);
- (7) an isolated polynucleotide (VII) comprising a 1884, 784, 1657, 2118, 2116, 2897, 839, 1081, 2924, 2781 or 754 base pair sequence (S2), fully defined in the specification, a naturally occurrence sequence having at least 90 % identity to (S2), its complement, or an RNA equivalent;
- (8) an isolated polynucleotide (VIII) comprising at least 60 contiguous nucleotides of (VII);
- (9) detecting (M1) a target polynucleotide having a sequence of (VII) in a sample, comprising:
 - (a) hybridizing the sample with a **probe** comprising at least 20 contiguous nucleotides of a sequence complementary to the target polynucleotide in the sample, the **probe** specifically hybridizes to the target polynucleotide under hybridizing conditions, and detecting the presence or absence of the hybridization complex, and, optionally, if present, the amount; or
 - (b) amplifying the target polynucleotide or its fragment using polymerase chain reaction amplification, and detecting the presence or absence of the amplified target polynucleotide or its fragment, and optionally, if present, the amount;

(10) **screening** (M2) a compound for effectiveness as an agonist or antagonist of (I) or for effectiveness in altering the expression of a target nucleotide having a sequence of (II), comprising:

(a) exposing a sample comprising (I) or the target nucleotide to the compound;

(b) detecting agonist or antagonist activity in the sample or the altered expression of the target nucleotide; and

(c) comparing the expression of the target polynucleotide in the presence of varying amounts of the compound and in the absence of the compound;

(11) **screening** (M3) for a compound that specifically binds to (I) or modulates the activity of (I), comprising:

(a) combining (I) with at least one test compound and detecting binding of (I) to the test compound, identifying a compound that specifically binds to (I), or

(b) assessing the activity of (I) in the test sample, and comparing the activity of (I) in the presence and absence of the test compound, a change in the activity of (I) in the presence of the test compound indicates a compound that modulates the activity of (I);

(12) a composition (IX) comprising (I), or an agonist or antagonist of (I) identified by M2; and

(13) assessing (M4) toxicity of a test compound, comprising:

(a) treating a biological sample containing nucleic acids with the test compound;

(b) hybridizing the nucleic acids of the treated biological sample with a **probe** comprising at least 20 contiguous nucleotides of (VII) under hybridizing conditions, the target polynucleotide comprising a polynucleotide sequence of (VII) or its fragment;

(c) quantifying the amount of hybridization complex; and

(d) comparing the amount of hybridization complex in the treated biological sample with the amount of hybridization complex in an untreated biological sample, a difference indicates the toxicity of the test compound.

ACTIVITY - Antiinflammatory; antidiarrheic; laxative; antiemetic; hepatotropic; anti-HIV (human immunodeficiency virus); antianemic; antiasthmatic; antiarteriosclerotic; antithyroid; immunosuppressive; antidiabetic; nephrotropic; antigout; thyromimetic; neuroprotective; osteopathic; uropathic; ophthalmological; antiarthritic; antirheumatic; dermatological; cytostatic; antibacterial; antifungal; protozoacide; tranquilizer; vulnerary; anticonvulsant; cerebroprotective; antiParkinsonian; nootropic; neuroleptic; antipsoriatic.

MECHANISM OF ACTION - Gene therapy.

No biological data is given.

USE - (IX) is useful for treating a disease or condition associated with decreased expression or overexpression of PPHKP. (I) or its fragments useful to screen for compounds that bind to (I) or modulate the activity of (I). (All claimed). (I) and (II) are useful in diagnosis, treatment and prevention of gastrointestinal disorders such as dysphagia, dyspepsia, indigestion, gastritis, anorexia, nausea pyrosis, gastroenteritis, hepatitis, Crohn's disease, Whipple's disease, Mallory-Weiss syndrome, irritable bowel syndrome, diarrhea, constipation, jaundice Wilson's disease, Reye's syndrome; immune system disorders such as acquired immunodeficiency syndrome (AIDS), Addison's disease, adult respiratory distress syndrome, anemia, asthma, atherosclerosis, autoimmune thyroiditis, diabetes mellitus, Good pasture's syndrome, gout, Grave's disease, Hashimoto's thyroiditis, multiple sclerosis, myasthenia gravis, osteoporosis, pancreatitis, Reiter's syndrome, rheumatoid arthritis, Sjogren's syndrome, systemic lupus erythematosus, Werner syndrome, bacterial, fungal, parasitic, protozoal, and helminthic infections, and trauma; neurological disorders such as epilepsy, stroke, Alzheimer's disease, Pick's disease, Huntington's disease, dementia, Parkinson's disease, kuru, Creutzfeldt-Jakob disease, and Gerstmann-Straussler-Scheinker syndrome, Tourette's disorder; and cell proliferative disorders

such as bursitis, cirrhosis, psoriasis, leukemia, lymphoma, melanoma, myeloma, sarcoma, and cancer. (I) is useful for analyzing the proteome of a tissue or cell type and for screening libraries of compound in various drug screening techniques. (II) is useful in somatic or germline gene therapy and in diagnosis of that diseases. (II) is useful for creating transgenic humanized animals (pigs) or transgenic animals (mice or rats) to model human diseases. (II) is useful for generating hybridization probes useful in mapping the naturally occurring genomic sequence. (VI) is useful for the diagnosis of disorders characterized by expression of PPHKP, or in assays to monitor patients being treated with PPHKP or agonist, antagonist or inhibitors of PPHKP. (VI) is useful as elements on a microarray which is useful to monitor or measure protein-protein interactions, drug-target interaction, and gene expression profiles.

Dwg.0/0

L27 ANSWER 14 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-202934 [20] WPIDS
 DNN N2001-144769 DNC C2001-060329
 TI Novel **protein** chip comprising several **probe proteins** fixed in a defined arrangement on a microsolid substrate useful for mass diagnosis or analysis of **target proteins** in test samples quantitatively or qualitatively.
 DC B04 D16 S03
 IN KIM, S Y; PARK, E J; YOON, G J; KIM, S; PARK, E; YOON, K
 PA (KIMS-I) KIM S Y; (DIAC-N) DIACHIP LTD
 CYC 94
 PI WO 2001014425 A1 20010301 (200120)* EN 59p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM
 DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC
 LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE
 SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 KR 2000071894 A 20001205 (200131)
 AU 2000067356 A 20010319 (200136)
 ADT WO 2001014425 A1 WO 2000-KR928 20000819; KR 2000071894 A KR 1999-34427
 19990819; AU 2000067356 A AU 2000-67356 20000819
 FDT AU 2000067356 A Based on WO 200114425
 PRAI KR 1999-34427 19990819
 AB WO 200114425 A UPAB: 20010410
 NOVELTY - **Protein** chip (I) for mass diagnosis or analysis of test samples (T), has microsolid substrate (MSS) on which many spots of **probe proteins** (II) are fixed in defined arrangement, is new. 0.1 pg of (II) which is an antigen, receptor or **enzyme** is fixed per spot on MSS via bonds between amino **groups** of (II) and **functional groups** of chemicals coated on MSS. (II) is capable of binding to **target proteins** in (T).
 DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
 (1) manufacturing (I) involves the following:
 (i) arraying mixtures of a coating buffer and one or more kinds of (II) at predetermined locations on MSS, with the quantity of the **proteins** per spot of 0.1 pg or more;
 (ii) immobilizing (II) by incubating the substrate at room temperature;
 (iii) fixing (II) on the substrate by immersing the substrate in 100% ethanol; and drying the substrate; and
 (2) an automated system (III) for diagnosing in several subjects comprises (I) and the following:
 (i) a first microarrayer capable of arraying one or more (II) in several spots on (I);
 (ii) the second microarrayer controlled to perform sequentially allotting test samples exactly to the locations at which (II) is fixed on

(I);

(iii) washing (I) after reaction, and adding secondary antibodies to react with **target proteins** in (T); and

(iv) a fluorescence microscope or a micro chip reader for detecting the reaction between (II) and the **target proteins**.

USE - (I) is useful for analyzing **target proteins** present in (T) quantitatively or qualitatively which involves:

(i) reacting (T) with (I);

(ii) washing (I);

(iii) reacting (I) obtained with fluorescence substance (preferably, fluorescein isothiocyanate (FITC))-conjugated secondary antibodies specific for a **target protein** which is capable of binding (II) fixed on (I); and

(iv) detecting the reaction signals with a fluorescence microscope or a microchip reader.

(I) In this case, has antigenic **proteins** relating to two or more diseases fixed in divided sectors on it, so that each sector contains **proteins** different from those on other sectors, (T) is serum of a subject and the reaction signals detected with a fluorescence microscope or a microchip reader refer to diagnostic indications for the diseases in the subject. Alternately, (I) comprises antigenic **proteins** relating to a disease and test samples are sera of two or more subjects, and the reaction signals detected with a fluorescence microscope or a microchip reader refer to diagnostic indications for the diseases in the subjects. Optionally, (I) comprises antigenic **proteins** relating to two or more diseases and test samples are sera of two or more subjects, and the reaction signals detected with a fluorescence microscope or a microchip reader refer to diagnostic indications for the diseases in the subjects. The third step of the method is performed by an automatic microarrayer system (claimed).

(I) has a wide range of applicability such as diagnosis of various kinds of metabolic diseases and viral or bacterial infections, and **screening** of antagonist useful for the development of new medicines different from the DNA chip used for the genetic analysis or diagnosis of diseases caused by genetic abnormalities. (I) in addition to clinical diagnosis can also be used in researches for the kinetics of **enzymatic** reactions and **screening** antagonist or **ligands** which binds to the receptors of interest.

ADVANTAGE - (I) enables multipurpose diagnosis of various diseases even with the small amount of samples for a number of subjects at a time, with a high throughput. (I) includes feasibility for automation and rapidity of the diagnostic processes, and possibility of constructing profiles of specific diseases. Many samples can be analyzed at a time with high accuracy. The chip can perform simultaneously the diagnosis of several diseases in a subject, of one disease in several subjects and of several diseases in several subjects. The highly integrated structure of (I) makes a biochemical or immunological assay faster suitable for automation, precise and easy to handle. The automatic diagnostic system using (I) is more efficient in terms of time, labor, and resources other than **enzyme** linked immunosorbant assay (ELISA) or chemiluminescence immunoassay (CLIA).

DESCRIPTION OF DRAWING(S) - The figure shows the genome of human immunodeficiency virus used in the method and the cloning regions of gag and env antigens present in it.

Dwg.1/13

L27 ANSWER 15 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-168291 [17] WPIDS

DNC C2001-050161

TI Preparing telechelic polymer, useful in crosslinked plastics synthesis or as **ligands** for cell surface receptors, comprises polymerizing monomer in presence of ruthenium or osmium carbene catalyst followed by reaction with capping agent.

DC A17 A96 B04 D16 E19
 IN KIESSLING, L L; STRONG, L E; GORDON, E J
 PA (WISC) WISCONSIN ALUMNI RES FOUND; (KIES-I) KIESSLING L L; (STRO-I) STRONG
 L E
 CYC 93
 PI WO 2000078821 A1 20001228 (200117)* EN 62p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG
 SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
 AU 2000066484 A 20010109 (200122)
 US 6271315 B1 20010807 (200147)
 US 6291616 B1 20010918 (200157)
 US 2002007016 A1 20020117 (200212)
 ADT WO 2000078821 A1 WO 2000-US40245 20000619; AU 2000066484 A AU 2000-66484
 20000619; US 6271315 B1 US 1999-335430 19990617; US 6291616 B1 US
 1999-336121 19990617; US 2002007016 A1 Div ex US 1999-335430 19990617, US
 2001-888098 20010622
 FDT AU 2000066484 A Based on WO 200078821; US 2002007016 A1 Div ex US 6271315
 PRAI US 1999-336121 19990617; US 1999-335430 19990617; US 2001-888098
 20010622
 AB WO 200078821 A UPAB: 20020114
 NOVELTY - Multivalent array is prepared by post-polymerization
 modification of a polymer backbone generated by a metal carbene-catalyzed
 ring opening metathesis polymerization (ROMP) system. The method comprises
 attaching desired pendant **functional groups** to
 preformed polymers prepared in the presence of ruthenium or osmium carbene
 catalyst(s).
 DETAILED DESCRIPTION - Preparing a telechelic polymer comprises:
 (i) polymerizing at least one monomer comprising at least one
 polymerizable group in the presence of at least one ruthenium or osmium
 carbene catalyst to form a polymer; and
 (ii) combining the polymer with at least one capping agent to react
 the polymer with the capping agent, where either the carbene catalyst, the
 capping agent or both are functionalized, to give a terminally
 functionalized polymer.
 INDEPENDENT CLAIMS are included for the following:
 (1) a library comprising a plurality of multivalent arrays where each
 multivalent array is prepared as above;
 (2) generating a library comprising a plurality of multivalent arrays
 comprising: (a) synthesizing each multivalent array as above; and (b)
 combining the multivalent array to generate a library;
 (3) a functionalized capping agent (FA) of formula (I');
 D = electron donating group;
 R6 = an organic group that includes a latent reactive group selected
 from an azide, a nitro group, a disulfide, a hydrazine, a hydrazide, a
 hydroxylamine, an aldehyde, a ketone, an epoxide, a cyano group, an
 acetal, a ketal, a carbamate, a thiocyanate, an activated ester and an
 activated acid;
 R7, R8 = H or an organic group;
 (4) a functionalized carbene of formula (III);
 M = Ru or Os;
 X, X' = anionic ligand; or
 X+X' = anionic bidentate ligand;
 L, L' = neutral ligand; or
 L+L' = bidentate neutral ligand;
 R4 = inorganic group that includes a latent reactive group selected
 from an azide, an epoxide, a cyano group, an acetal, a ketal, a carbamate,
 a thiocyanate, an activated ester, an activated acid, a hydrazine and a
 hydrazone;
 (5) solid-supported functionalized carbene of formula (V);

R' = H or an organic group;

LK = cleavable linker to a solid support;

(6) a method of preparing a multivalent array;

(7) polymer templates of formula (VII) and (VIII);

BB = backbone repeat unit which may be cyclic or acyclic, and may be the same or different in a random or block arrangement;

R1', R2' = H or an organic group, which may be connected such that they form a ring;

provided that at least one of R1' and R2' includes a protected amine or an activated ester;

R4'-R7' = H or organic group;

Z = H, halide, hydroxyl, thiol or amine;

n = average number of repeating monomer units;

(8) a kit comprising the polymer template (VIII) and instruction means for using functionalizing reagent to attach a pendant functional group to the polymer template;

(9) a library which comprises a plurality of multivalent arrays.

USE - For synthesizing multivalent arrays and combinatorial libraries of multivalent arrays such as functionalized polymers (including short oligomers), libraries of oligomeric substances that differ in type and number of functional groups, terminal functionality and in length. The functionality may include those which allow for immobilization on a substrate, are capable of fluorescence allowing for the creation of a molecular probe that can be used to visualize a receptor-ligand interaction on a cell surface. For synthesizing multivalent arrays of biologically relevant binding epitopes. Multivalent arrays have applications in fields such as pharmaceuticals, medical devices, sensors and optical materials, especially in medical and biotechnology areas where the binding of cell surface receptors to particular epitopes of multivalent arrays can trigger a wide variety of biological responses. Multivalent arrays induce the release of a cell surface protein. Libraries of multivalent arrays are useful in screening and selection of multivalent arrays that exhibit a desired function, especially libraries for screening for various biological activities (e.g. cell surface binding, biological signal effects etc.). In protein-carbohydrate recognition processes, multivalent saccharide-substituted arrays can exhibit increased avidity, specificity, and unique inhibitory potencies under dynamic shear flow conditions. Due to their ability to span large distances, linear multivalent arrays of varying length and epitope density are particularly useful for probing structure-function relationships in biological systems. For producing random copolymers and block copolymers. Attached functional groups may provide a recognition element (i.e. binding site) for biological entity e.g. cell surface receptor or it may be generally unreactive so that the resultant polymers may be bioactive or biocompatible. Telechelic polymers are useful in the synthesis of crosslinked plastics.

ADVANTAGE - Unlike conventional ROMP methods that incorporate the desired pendant functional groups into the monomers followed by polymerization, the present methods attach the desired pendant functional groups to preformed polymers which provide better control and access to wider variety of materials than previous methods and give rise to materials with unique surfaces or ligands for a wide variety of natural and synthetic receptors. The present methods provide ability to control the number, type and position of pendant functional groups as well as selected functionality at the polymer ends. The method allows generation of block copolymers where the length of each block of monomers can be controlled. The present method of block copolymer formation allows formation of polymers with selected spacing between functional groups, allows synthesis of multivalent arrays of defined length, defined density of functional groups, defined distance between functional groups, defined combination of different functional groups (relative number and spacing), defined position of the same or different functional groups and defined groupings of functional groups. Further disadvantage of the conventional

methods avoided by the present method include having to synthesize a new functionalized cyclic olefin monomer for each polymer class to be produced. The physical properties of each monomer e.g. its solubility, electron density and strain of the cyclic olefin result in different rates of initiation, propagation and non-productive termination of the reaction, and purification of the desired products can be complicated, which all hinder large-scale syntheses of multivalent arrays. In contrast, terminal attachment of functional groups to preformed polymer backbone generated by a metal carbene-catalyzed ROMP system facilitates purification, allowing its use in large-scale production. Preferred methods of the present process give relatively high yields, are convenient and/or efficient in the preparation of polymers of e.g. varying average lengths, varying epitope density and varying functionality.

Dwg.0/16

L27 ANSWER 16 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-159282 [16] WPIDS
 DNN N2001-116091 DNC C2001-047292
 TI Platform for use in analyzing samples simultaneously, comprises an optically transparent substrate having a refractive index (n_1), and a thin, optically transparent layer having a greater refractive index than n_1 .
 DC A89 B04 D16 J04 S03
 IN BUDACH, W E G; NEUSCHAEFER, D
 PA (NOVS) NOVARTIS AG
 CYC 93
 PI WO 2001002839 A1 20010111 (200116)* EN 69p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
 NL OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000058243 A 20010122 (200125)
 ADT WO 2001002839 A1 WO 2000-EP6238 20000703; AU 2000058243 A AU 2000-58243
 20000703
 FDT AU 2000058243 A Based on WO 200102839
 PRAI GB 2000-11420 20000511; GB 1999-15703 19990705
 AB WO 200102839 A UPAB: 20010323
 NOVELTY - A platform for use in sample analysis comprising an optically transparent substrate having a refractive index (n_1), and a thin, optically transparent layer, which is formed on one surface of the substrate, having a refractive index (n_2) greater than n_1 , is new.
 DETAILED DESCRIPTION - A new platform has incorporated corrugated structures comprising periodic grooves which define sensing areas or regions, each for capture elements. The grooves are profiled, dimensioned and oriented so that either:
 (a) coherent light incident on the platform is diffracted into individual beams or diffraction orders which interfere resulting in the reduction of the transmitted beam and an abnormal high reflection of the incident light, thus generating an enhanced evanescent field at the surface of the sensing areas; or
 (b) coherent and linearly polarized light incident on the platform is diffracted into individual beams or diffraction orders which interfere resulting in almost total extinction of the transmitted beam and an abnormal high reflection of the incident light, thus generating an enhanced evanescent field at the surface of the sensing areas.
 INDEPENDENT CLAIMS are also included for the following:
 (1) an apparatus for analyzing samples comprising a platform, for generating a light beam and for directing the beam so that it is incident upon the platform at an angle which causes evanescent resonance to occur in the platform, thus creating an enhanced resonant field in the sensing area of the platform, and for detecting a characteristic of a material

disposed on or in the vicinity of the sensing area of the platform; and
 (2) analyzing sample(s) by bringing the sample into contact with the sensing area of a platform, irradiating the platform with a light beam such that evanescent occurs within the sensing area of the platform, and detecting radiation emanating from the sensing area.

USE - The platform is useful in sample analysis. The process may be used in one or more of the following: gene expression, genomics, pharmacogenomics, toxicogenomics, toxicoproteomics, genetics, pharmacogenetics, toxicogenetics, exon/intron expression profiling, human leukocyte antigens (HLA) typing, analysis of splicing variants, **proteomics** (on-chip **protein** assays), patient monitoring (drug, metabolites, and markers), point-of-care personalized medicine, diagnostics, on-chip 2d gels for **proteomics**, single nucleotide polymorphism mini-sequencing, high throughput screening, combinatorial chemistry, **protein-protein** interaction, molecular interaction, chip-based **protein**-antibody and peptide interaction, green fluorescent **protein**, in-situ hybridization, confocal microscopy, fluorescence correlation spectroscopy, conventional microscopy, and MALDI-TOF MS (mass spectroscopy) (all claimed).

ADVANTAGE - Compared with previous techniques of analyzing samples, the new method allows multiple samples to be analyzed simultaneously in an extremely sensitive, reliable and quantitative manner. Luminescence crosstalk and local light intensities are well defined, and true multiplexing is allowed. The method is simple and requires solely simple adjustment of the angle of incident light beam.

DESCRIPTION OF DRAWING(S) - The figure shows an apparatus for analyzing optical parameters and evanescent resonance condition of a platform.

glass substrate 30
 grooves 31
 optically transparent metal oxide layer 32
 grooves 33
 Dwg.2/10

L27 ANSWER 17 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2001-060972 [07] WPIDS
 DNC C2001-016756
 TI Oligomers comprising L-ribo-Locked Nucleic Acid (LNA) nucleosides, useful for therapeutic purposes e.g. in the construction of oligonucleotides, as substrates for nucleic acids polymerases and in RNA mediated catalytic processes.
 DC B05 D16
 IN WENGEL, J
 PA (EXIQ-N) EXIQON AS
 CYC 92
 PI WO 2000066604 A2 20001109 (200107)* EN 79p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
 EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
 LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
 SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 2000043918 A 20001117 (200111)
 ADT WO 2000066604 A2 WO 2000-DK225 20000504; AU 2000043918 A AU 2000-43918
 20000504
 FDT AU 2000043918 A Based on WO 200066604
 PRAI DK 2000-32 20000111; DK 1999-603 19990504; DK 1999-1225
 19990901
 AB WO 200066604 A UPAB: 20010202
 NOVELTY - An oligomer comprising L-ribo-LNA nucleoside analogs (I) is new.
 DETAILED DESCRIPTION - An oligomer comprising L-ribo-LNA nucleoside analogs of formula (I) is new.
 $X = O, S, -N(RN'')-$ or $-C(R6R6'')-$;

B = 1-4C alkoxy, 1-4C alkyl, 1-4C acyloxy (all optionally substituted), H, OH, nucleobases, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups, reporter groups or ligands;

P = a radical position for an internucleoside linkage to a succeeding monomer, or a 5'-terminal group, both optionally substituted by R5 or R5'';

P' = an internucleoside linkage to a preceding monomer, or a 3'-terminal group;

R2'', R4'' = biradicals consisting of 1-4 groups/atoms selected from -C(RaRb)-, -C(Ra)=C(Ra)-, -C(Ra)=N-, O, -Si(Ra)2-, S, SO2, -N(Ra)- or -(C=Z);

Z = O, S or -N(Ra)-;

Ra, Rb = e.g. H, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl (all optionally substituted), OH, 1-12C alkoxy, 2-12C alkenyloxy, carboxy, 1-12C alkoxycarbonyl, 1-12C alkylcarbonyl, formyl, aryl, aryloxycarbonyl, aryloxy, arylcarbonyl, heteroaryl, amino, mono- or di-(1-6C alkyl)-amino, carbamoyl, or where two geminal substituents Ra and Rb together may designate optionally substituted methylene olefin (=CH2);

R1'', R2, R3'', R5, R5'', R6, R6'' = e.g. H, 1-12C alkyl, 2-12C alkenyl, 2-12C alkynyl (all optionally substituted), OH, 1-12C alkoxy, 2-12C alkenyloxy, carboxy, 1-12C alkoxycarbonyl, 1-12C alkylcarbonyl, formyl or aryl

RN = H or 1-4C alkyl and where two adjacent (non-geminal) substituents may designate an additional bond resulting in a double bond; and

RN'' = H or 1-4C alkyl;

INDEPENDENT CLAIMS are also included for:

(1) nucleoside analog monomers of formula (II);

(2) conjugates of L-ribo-LNA modified oligonucleotides and proteins, amplicons, enzymes, polysaccharides, antibodies, haptens, peptides or PNA;

(3) A kit for the isolation, purification, amplification, detection, quantification or capture of natural or synthetic nucleic acids comprising a reaction body and one or more L-ribo-LNA modified oligonucleotides (oligomer).

Q, Q'' = H, N3, halo, CN, NO2, OH, Prot-O-, Act-O-, SH, Prot-S, Act-S-, 1-6C alkylthio, NH2, Prot-N(RH)-, Act-N(RH)-, mono or di-(1-6C alkyl)-amino, or 1-6C alkoxy, 1-6C alkyl, 2-6C alkenyl, 2-6C alkenyloxy, 2-6C alkynyl or 2-6C alkynyloxy (all optionally substituted), monophosphate, diphosphate, triphosphate, DNA intercalator, photochemically active group, thermochemically active group, chelating group, reporter group, ligand, COOH, sulfono, CH2OH, Prot-O-CH2-, Act-O-CH2-, CH2NH2, Prot-N(RH)-CH2-, Act-N(RH)-CH2-, COOMe or sulfonomethyl;

Prot = protecting group for -OH, SH, or -NH(RH) respectively;

Act = activating group for -OH, -SH, or (NH(RH)) respectively;

RH = H or 1-6C alkyl;

R2'', R4'' = O, -(CR''R'')r+s+1-, -(CR''R'')r-O-(CR''R'')s-, -(CR''R'')r-S-(CR''R'')s-, -(CR''R'')r-N(R'')-(CR''R'')s-, -O-(CR''R'')r+s-O-, -S-(CR''R'')r+s-O-, -O-(CR''R'')r+s-S-, -N(R'')-(CR''R'')r+s-O-, -O-(CR''R'')r+s-N(R'')-, -S-(CR''R'')r+s-S-, -N(R'')-(CR''R'')r+s-N(R'')-, -N(R'')-(CR''R'')r+s-S- or -S-(CR''R'')r+s-N(R'')-;

R'' = H, halo, N3, CN, NO2, OH, SH, NH2, mono- or di-(1-6C alkyl)-amino, optionally substituted 1-6C alkoxy, optionally substituted 1-6C alkyl, DNA intercalators, photochemically active groups, thermochemically active groups, chelating groups reporter groups or ligands or R''-C-C-R'' = a bond;

r, s = 0 to 3 provided that r+s = 1 to 4;

with the proviso that any chemical group (including any nucleobase) which is reactive under the conditions prevailing in oligonucleotide synthesis, is optionally functional group protected.

Full definitions are given in the Definition FULL DEFINITIONS field.

ACTIVITY - No relevant biological data is included.

MECHANISM OF ACTION - None given.

USE - (I) are useful for preparation of the **conjugates** of the L-ribo-LNA modified oligonucleotides (oligomers), as a substrate for **enzymes** active on nucleic acids e.g. DNA and RNA polymerases, for therapeutic or diagnostic purposes, in the construction of a solid surface onto which LNA modified oligonucleotides of different sequences are attached, in the sequence specific cleavage of target nucleic acids, in various therapies e.g. antisense, antigene or gene activating therapy. Complexes of more than one L-ribo-LNA modified nucleotide are also useful for these therapies.

(I) is useful as an aptamer in molecular diagnostics and in RNA mediated catalytic processes, as an aptamer in specific binding of antibiotics, drugs, amino acids, peptides, structural **proteins**, **protein receptors**, **protein enzymes**, saccharides, polysaccharides, biological cofactors, nucleic acids or triphosphates, as an aptamer in the separation of enantiomers by stereospecific binding, for the labelling of cells or to hybridize to non-**protein** coding cellular RNAs, e.g. tRNA, rRNA, snRNA and scRNA in vitro or in vivo.

(I) may be used in the construction of an oligonucleotide comprising a fluorophor and a quencher, positioned in such a way that the hybridized state of the oligonucleotide can be distinguished from the unbound state of the oligonucleotide by an increase in the fluorescent signal from the probe. (I) may be used for purification of, and capture and detection, of naturally occurring doubly stranded or single stranded nucleic acids e.g. DNA or RNA.

The L-ribo-LNA modified oligonucleotide (I) is used in diagnostics e.g. for the isolation, purification, amplification, detection, identification, quantification or capture of natural or synthetic nucleic acids (all claimed).

ADVANTAGE - The oligomers comprising L-ribo-Locked Nucleic Acid (LNA) nucleosides have high affinity for complementary nucleic acids. Use of the alpha -L-ribo-LNA may allow targeting of tRNAs, rRNAs, snRNAs and scRNAs, thus allowing their use as antisense targets. When derivatives of L-ribo-LNAs are incorporated into partly modified oligonucleotides, they decrease the affinity of these modified oligonucleotides for both complementary DNA and RNA compared to the unmodified nucleotides. However, when incorporated into fully L-ribo-LNA modified oligonucleotides, a dramatic increase in hybridization properties for both complementary ssDNA and ssRNA is observed. The alpha -L-ribo-LNA, a special variant of the L-ribo-LNAs, in addition to the described properties, has an ability to discriminate between RNA and DNA targets when hybridizing. Depending on the application, the use of fully modified L-ribo-LNA nucleotides thus offers the possibility of either greatly increasing the affinity of a standard oligonucleotide without compromising specificity, significantly increasing the specificity without compromising affinity or specifically hybridizing to RNA targets.

Dwg.0/4

L27 ANSWER 18 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2000-423449 [36] WPIDS
 DNC C2000-128268
 TI Composition for identifying target sequence of nucleic acids for detecting genetic-diseases and pathogens in food and water, comprises non-nucleotide **probe** which sequence specifically hybridizes to target sequence.
 DC B04 D16 J04
 IN COULL, J M; FIANDACA, M J; HYLDIG-NIELSEN, J J; JOHANSEN, J T
 PA (BOST-N) BOSTON PROBES INC
 CYC 73
 PI WO 2000034521 A1 20000615 (200036)* EN 82p

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW

W: AL AU BA BB BG BR CA CN CU CZ EE GE HU IL IN IS JP KP KR LC LK LR
 LT LV MG MK MN MX NO NZ PL RO SG SI SK SL TR UA US UZ VN YU

AU 2000017514 A 20000626 (200045)

EP 1137807 A1 20011004 (200158) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI

ADT WO 2000034521 A1 WO 1999-US28966 19991208; AU 2000017514 A AU 2000-17514
 19991208; EP 1137807 A1 EP 1999-960659 19991208, WO 1999-US28966 19991208

FDT AU 2000017514 A Based on WO 200034521; EP 1137807 A1 Based on WO 200034521

PRAI US 1998-111439P 19981208

AB WO 200034521 A UPAB: 20000801

NOVELTY - A composition (I) comprising a matrix, a nucleic acid molecule (NA) comprising a target sequence which is electrostatically bound to the matrix under suitable electrostatic binding conditions and a non-nucleotide probe comprising a probing nucleobase sequence which is sequence specifically hybridized to a portion of one or more target sequences, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a method for the detection, identification or quantitation of a target sequence (or of two or more target sequences) of a (or one or more) nucleic acid molecule(s) in a sample comprising:

(i) contacting the sample with a matrix and at least one (or two independently detectable non-) nucleotide probe(s);

(a) where the nucleic acid molecule(s) will electrostatically bind to the matrix under suitable electrostatic binding conditions; and

(b) where the non-nucleotide probe(s) will hybridize, under suitable hybridization conditions to at least a portion of the target sequence if present in the sample; and

(ii) detecting, identifying or quantitating the non-nucleotide probe/target sequence complex as a means to detect, identify or quantitate the (or each) target sequence in the sample;

(2) a method for the detection, identification or quantitation of a target sequence of a nucleic acid molecule in a sample comprising:

(a) contacting the sample with at least one non-nucleotide probe where the non-nucleotide probe will hybridize, under suitable hybridization conditions, to at least a portion of the target sequence if present in the sample;

(b) contacting the sample with a matrix where the nucleic acid molecule will electrostatically bind to a matrix under suitable electrostatic binding conditions;

(c) contacting the sample with one or more enzymes capable of degrading sample contaminates including the nucleic acid molecule but not the non-nucleotide probe/target sequence complex at a timer after performing step (a); and

(d) detecting, identifying or quantitating the non-nucleotide probe/target sequence complex at a time after performing in (b) as a means to detect, identify or quantitate the target sequence in the sample;

(3) a method for the detection, identification or quantitation of a target sequence of a nucleic acid molecule electrostatically immobilized at a location on an array comprising nucleic acid molecules electrostatically bound at unique locations comprising:

(a) contacting the array with at least one non-nucleotide probe which will hybridize, under suitable hybridization conditions to at least a portion of the target sequence if present on the array; and

(b) detecting, identifying or quantitating the non-nucleotide probe/target sequence complex electrostatically bound at a unique location on the array as the means to determine the presence, absence or

amount of target sequence present at the unique array location;

(4) a method for the detection, identification or quantitation of a target sequence of a nucleic acid molecule which may be present in any of 2 or more samples of interest, comprising:

(a) mixing each of the two or more samples of interest with at least one non-nucleotide probe under suitable hybridization conditions;

(b) contacting a matrix under suitable electrostatic binding conditions with at least a portion of each of the two or more samples to therefore electrostatically immobilize the nucleic components of each sample to the matrix, each at a unique location and therefore creating a matrix array of samples; and

(c) detecting, identifying or quantitating the non-nucleotide probe/target sequence complex which is electrostatically bound at a unique location on the matrix sequence in each of the two or more samples; and

(5) a kit for the analysis of a sample containing a nucleic acid molecule comprising a target sequence comprising a matrix and at least one non-nucleotide probe having a probing nucleobase sequence which sequence specifically hybridizes under suitable hybridization conditions, to at least a portion of the target sequence sought to be detected.

USE - (I) is useful for detecting, identifying or quantitating a target sequence of a NA in a sample by contacting the sample with (I) and detecting the non-NT probe/TA complex in the sample. The assay is used to detect, identify or quantitate one or more single point mutations present in a NA, where one or more non-target probes are added to the assay to improve the single point mutation discrimination of the assay. (I) is also useful for distinguishing single point mutations in one or more NAs which may be present any of two or more samples. (II) is useful for detecting organisms in food, beverages, water, pharmaceutical products, personal care products, daily products, environmental samples and to test raw materials products or processes.

(II) is also useful to perform a homogeneous assay, to examine clinical samples such as specimens or equipment, fixtures and products used to treat humans or animals and to detect a TA specific for a genetically based disease and in forensic technique such as prenatal screening, paternity testing, identity confirmation or crime investigation (all claimed).

ADVANTAGE - The method is rapid, sensitive, reliable and versatile in detecting target sequences which are particular to organisms found in food, beverages, water and pharmaceutical products. Non-nucleotide probe/TA is protected against degradation by enzymes and hence the sample can be treated with enzymes to degrade sample contaminants. The method facilitates simple processing and analysis of samples, particularly complex biological samples under wide range of assay conditions.

Dwg.0/6

L27 ANSWER 19 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 2000-412037 [35] WPIDS

DNN N2000-308007 DNC C2000-124869

TI New electrically conductive, electroactive functionalized conjugated polypyrroles are useful as scavengers for biological ligands and for detecting and assaying biological ligands

DC A26 A96 B04 D16 E19 S03 X12

IN GARNIER, F

PA (INMR) BIO MERIEUX

CYC 21

PI WO 2000031750 A1 20000602 (200035)* EN 63p

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE

W: CA JP

EP 1138048 A1 20011004 (200158) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 ADT WO 2000031750 A1 WO 1999-IB1947 19991118; EP 1138048 A1 EP 1999-972771
 19991118, WO 1999-IB1947 19991118
 FDT EP 1138048 A1 Based on WO 200031750
 PRAI US 1998-195544 19981119
 AB WO 200031750 A UPAB: 20000725
 NOVELTY - An electrically conductive, electroactive functionalized conjugated polymer (I') is new.
 DETAILED DESCRIPTION - An electrically conductive, electroactive functionalized conjugated polymer of formula (I') is new.
 n, p = 0 or integer;
 R = H or group able to bond with a biological molecule or antiligand (C(O)O-(N-hydroxyphthalimide), C(O)O-(pentafluorophenol), electrochemical probe optionally bound to an activated ester) provided that at least one is a functional group and they are not all CH₂C(O)OH; and
 Y' = coupling arm.
 An INDEPENDENT CLAIM is included for an electrically conductive, electroactive functionalized conjugated polymer of formula (II').
 R' = H or a functional group able to bond with a biological molecule (polynucleotide or peptide sequence) or antiligand (C(O)O-(N-hydroxyphthalimide), C(O)O-(pentafluorophenol), electrochemical probe optionally bound to an activated ester).
 provided that at least one R' is a functional group covalently bound to a biological molecule or antiligand.
 USE - The polymers are useful as scavengers for biological ligands and for detecting and assaying biological ligands (e.g. polynucleotides and enzymes especially carboxypeptidase A) and may be deposited on a conductive substrate or be in the form of a self-supporting film or electrode.
 ADVANTAGE - The polypyrroles allow preparation of electroactive and conductive polymers which are several millimeters thick thereby allowing a great density of functional sites and improved sensitivity.
 Dwg. 0/15

L27 ANSWER 20 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 2000-399281 [34] WPIDS
 DNC C2000-120488
 TI Modulating the activity of I-kappaB kinases or cyclic nucleotide phosphodiesterases for the treatment of inflammatory disorders, autoimmune disorders (e.g. diabetes and Crohn's disease) and depression.
 DC B04 B05
 IN ARKHAMMAR, P O G; BJORN, S P; SCUDDER, K M; TERRY, B R; THASTRUP, O
 PA (BIOI-N) BIOIMAGE AS
 CYC 91
 PI WO 2000023091 A2 20000427 (200034)* EN 128p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ TZ UG ZW
 W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES
 FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS
 LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL
 TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
 AU 9961899 A 20000508 (200037)
 EP 1146888 A2 20011024 (200171) EN
 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
 RO SE SI
 ADT WO 2000023091 A2 WO 1999-DK567 19991015; AU 9961899 A AU 1999-61899
 19991015; EP 1146888 A2 EP 1999-948735 19991015, WO 1999-DK567 19991015
 FDT AU 9961899 A Based on WO 200023091; EP 1146888 A2 Based on WO 200023091
 PRAI DK 1998-1323 19981015; DK 1998-1321 19981015; DK 1998-1322
 19981015

AB WO 200023091 A UPAB: 20000718

NOVELTY - A method (A) for modulating the specific effectiveness of I-kappaB kinases or cyclic nucleotide phosphodiesterases which have the ability to cleave cyclic AMP and/or GMP (adenosine and guanine monophosphate, respectively), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) the use (I) of a substance, capable of modulating the specific effectiveness of a cyclic nucleotide phosphodiesterase or I-kappaB kinases through modulating the spatial distribution (or a change in spatial distribution) of the cyclic nucleotide phosphodiesterase or I-kappaB kinases within the cells of an animal, for the preparation of a pharmaceutical for the prevention and/or treatment of an adverse condition in an animal that may be reduced or abolished by modulating the activity of 1 or more cyclic nucleotide phosphodiesterase or I-kappaB kinases with the ability to cleave cyclic AMP (adenosine monophosphate) or cyclic GMP (guanine monophosphate) or by modulating the activity of 1 or more I-kappaB kinases;

(2) a method (II) for extracting quantitative information relating to an influence on a cellular response, comprising recording variation caused by the influence on a mechanically intact living cell (or cells) in spatially distributed light emitted from an luminophore (the luminophore is part of a fluorescent probe further comprising at least a part of a cyclic nucleotide phosphodiesterase or I-kappaB kinase, the fluorescent probe is present within the cells and is capable of being redistributed in a manner related to the degree of influence and/or of being modulated by a component capable of being redistributed in a manner related to the degree of influence, the association resulting in a modulation of the luminescence characteristics of the luminophore) and processing the recorded variation in the spatially distributed light to provide quantitative information correlating the spatial distribution to the degree of influence on the cellular response;

(3) a screening assay (III) for carrying out the method (II); and

(4) a nucleotide sequence (IV) encoding a polypeptide corresponding to amino acids 331-552 of a defined 552 amino acid sequence (A) given in the specification (or any 25 contiguous amino acid subsequence of that sequence) able to dislocate I-kappaB kinase when expressed in CHO (Chinese hamster ovary) cells under the control of the CMV (cytomegalovirus) promoter.

ACTIVITY - Antiinflammatory; antiasthmatic; antirheumatic; antiulcer; immunosuppressant; antidiabetic; dermatological; antithyroid; antibacterial; antidepressant.

MECHANISM OF ACTION - I-kappaB kinase and/or cyclic nucleotide phosphodiesterase modulator.

USE - (I) is used to prevent or treat diseases that may be reduced or abolished by modulating the activity of 1 or more cyclic nucleotide phosphodiesterase having the ability to cleave cyclic AMP or GMP (adenosine or guanine monophosphate) or by modulating the activity of 1 or more i-kappaB kinases. This involves modulating the specific effectiveness of the cyclic nucleotide phosphodiesterase or I-kappaB kinase by modulating the spatial distribution within cells of the animal. If the cyclic nucleotide phosphodiesterase used is a PDE3, PDE7, PDE8 or a splice variant of PDE4, (I) is used to treat inflammatory diseases such as chronic inflammation (CI) (especially CI airway diseases such as asthma and chronic bronchial hyper-reactivity of non-asthma etiology, CI joint disorders such as rheumatoid arthritis and pellagra and CI bowel diseases such as ulcerative colitis and Crohn's disease), autoimmune diseases associated with CI (such as rheumatoid arthritis, diabetes mellitus type I, systemic lupus erythematosus, myasthenia gravis, Hashimoto's thyroiditis, Grave's disease and immune thrombocytopenic purpura), disregulations of the immune system (such as acute respiratory distress syndrome (ARDS) and septic shock) and/or depression.

Alternatively, if the cyclic nucleotide phosphodiesterase is PDE1, PDE2, PDE6, PDE9, PDE10 or a splice variant of PDE5, (I) is used to treat hypo- or hypertension, erectile dysfunction, circadian rhythm resetting or jet-lag. (I) is preferably used to treat a mammal, especially a human being (claimed).

Dwg.0/3

L27 ANSWER 21 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1999-580156 [49] WPIDS
 CR 2000-052620 [54]
 DNC C1999-168749
 TI New bioreagents comprising dendrimers, used for bioassays such as DNA assays, immunoassays or **protein-ligand** interactions.
 DC A11 A96 B04 D16 J04 K08
 IN DRUKIER, A K; WILK, A
 PA (BIOT-N) BIOTRACES INC
 CYC 84
 PI WO 9943287 A2 19990902 (199949)* EN 52p
 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
 OA PT SD SE SL SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD
 GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
 UA UG US UZ VN YU ZW
 AU 9927880 A 19990915 (200004)
 ADT WO 9943287 A2 WO 1999-US4068 19990225; AU 9927880 A AU 1999-27880 19990225
 FDT AU 9927880 A Based on WO 9943287
 PRAI US 1998-75859P 19980225
 AB WO 9943287 A UPAB: 20011203
 NOVELTY - New bioreagents for analytes comprise a linker arm forming moieties and reporter moieties on terminal branches
 DETAILED DESCRIPTION - (A) A novel bioreagent which is a SuperTracer for an analyte of interest which has been labeled, comprises:
 (1) a linker arm moiety;
 (2) at least one forking moiety provided on the linker arm moiety and having terminal branches; and
 (3) at least one reporter moiety provided on respective terminal branches of the at least one forking moiety, where the bioreagent:
 (a) conjugates a predetermined number of labels;
 (b) conjugates to biopolymers by use of the linker arm, and
 (c) has a nonspecific biological background (NSBB) which is lower than 10 attomole/well of a microtiter plate.
 INDEPENDENT CLAIMS are also included for the following:
 (1) an assay for direct DNA quantitation comprising:
 (a) providing a bioreagent as in (A) which is a SuperTracer;
 (b) conjugating the bioreagent with a primary hybridization probe, which is preferably an oligonucleotide having a length ranging from 10 to 200 bases, to provide a conjugate; and
 (c) subjecting target DNA to the conjugate;
 (2) a bioreagent having a structure: (linker)1 + (switch)i + (linker)2 + SuperTracer (structure (I)); where (linker)1, (linker)2 and SuperTracer are polymers;
 (3) a method for improving immunoassay sensitivity to improve the limits of detection (LOD) comprising at least one of:
 (a) using secondary antibodies in parallel to increase signal;
 (b) using a SuperTracer to amplify signal;
 (c) using a multi photon detection (MPD) instrumentation to quantitate signals at sub-attomole levels;
 (d) using a technique to diminish NSBB, preferably an exponential wash; and
 (e) using a releasable (Switch) to permit independent quantitation of remaining NSBB;
 (4) an immunoassay having improved lod using a SuperTracer with an

oligonucleotide linker and which comprises:

- (a) capturing a target on a solid-surface using an antibody Ab1;
 - (b) stringent washing;
 - (c) conjugating to the captured target of (Ab2 + DNA) construct;
 - (d) stringent washing;
 - (e) blocking using a blocker, preferably a noniodinated SuperTracer;
 - (f) stringent washing;
 - (g) adjusting at least one of pH and temperature to levels for DNA hybridization;
 - (h) applying a radiolabeled SuperTracer with DNA linker(s);
 - (i) stringent washing; and
 - (j) quantitating using MPD instrumentation;
- (5) a kit of bioreagents of structure (I) where (linker)1, (linker)2 and SuperTracer are polymers and are always the same constituent, respectively, where only (switch)i is a variable constituent, and where the linkers can be implemented in ways which include either as a chain of polypeptides or as oligonucleotides;
- (6) a bioreagent with high affinity for an analyte of interest comprising:
- (a) a linker arm terminal moiety, R1 which has an affinity for the analyte of interest;
 - (b) a linker arm which is a polymer having a chain length to mitigate steric interference between R1 and a forking moiety;
 - (c) a forking moiety comprised of a substance having a spherical branched polymer structure including terminal functional groups; and
 - (d) at least one reporter moiety, R2, provided on respective terminal functional groups of the forking moiety.

USE - The bioreagents can be used in bioassays, including DNA assays, immunoassays and protein-ligand interactions.

ADVANTAGE - The bioreagents provide extraordinary signal amplification, e.g. allowing fast measurement of a single copy or a few copies of DNA. They can provide assays capable of attamole sensitivity with low NSBB.

Dwg.0/12

L27 ANSWER 22 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1999-458483 [38] WPIDS
 DNN N1999-342931 DNC C1999-134644
 TI Conducting assay of sample containing analyte using metal-ligand complexes for life-timebased sensing, a display of polarized emission, increased emission and photosensitivity.
 DC B02 B04 D16 S03
 IN CASTELLANO, F; LAKOWICZ, J R; MURTAZA, Z
 PA (LAKO-I) LAKOWICZ J R
 CYC 21
 PI WO 9936779 A1 19990722 (199938)* EN 88p
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: CA JP
 US 6214628 B1 20010410 (200122)

ADT WO 9936779 A1 WO 1999-US774 19990114; US 6214628 B1 US 1998-7167 19980114
 PRAI US 1998-7167 19980114

AB WO 9936779 A UPAB: 19990922

NOVELTY - A method for conducting an assay of a sample containing an analyte of interest, comprises:

- (a) forming a mixture to bring a metal-ligand complex into interactive proximity with the sample containing an analyte of interest;
- (b) irradiating the mixture with electromagnetic light energy; and
- (c) measuring the emitted light and utilizing the measurement of the emitted light to measure the analyte of interest.

DETAILED DESCRIPTION - A method for conducting an assay of a sample containing an analyte of interest, comprises:

- (a) forming a mixture to bring a metal-ligand complex into

interactive proximity with the sample containing an analyte of interest;

(b) irradiating the mixture with electromagnetic light energy to cause a emission of light indicative of the analyte of interest; and

(c) measuring the emitted light and utilizing the measurement of the emitted light to measure the analyte of interest.

An INDEPENDENT CLAIM is also included for a metal-ligand complex of the formula, $(Re(bcp)(CO)_3(4-COOHPy))_+$.

USE - The assay is useful for assaying a sample containing an analyte of interest for use in biophysics, clinical chemistry and immunoassays (especially fluorescence polarization for the analysis of biological systems e.g. the study of entire cells, viruses and other large macromolecules and complexes. It is also applicable to red fluorescent dyes for biophysics and for sensors and for studying hydrodynamics of molecules.

ADVANTAGE - The metal-ligand complexes allow life-time based sensing with low cost instrumentation. Lanthanide chelate compounds have longer decay times to allow gated detection and increased sensitivity for immunoassays and increased photostability in solvents.

Dwg.0/30

L27 ANSWER 23 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1999-357694 [30] WPIDS
 DNC C1999-105815
 TI Psoralen compounds and their salts, e.g. 3-(4-amino-2-oxa)butyl-4,4'-8-trimethyl-psoralen.
 DC B02 B04 D22
 IN NERIO, A; WOLLOWITZ, S
 PA (CERU-N) CERUS CORP
 CYC 23
 PI WO 9926476 A1 19990603 (199930)* EN 53p
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: AU CA JP
 AU 9915929 A 19990615 (199944)
 EP 1032265 A1 20000906 (200044) EN
 R: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
 US 6133460 A 20001017 (200054)
 ADT WO 9926476 A1 WO 1998-US24709 19981120; AU 9915929 A AU 1999-15929
 19981120; EP 1032265 A1 EP 1998-960295 19981120, WO 1998-US24709 19981120;
 US 6133460 A Provisional US 1997-66224P 19971120, US 1998-196935 19981120
 FDT AU 9915929 A Based on WO 9926476; EP 1032265 A1 Based on WO 9926476
 PRAI US 1998-196935 19981120; US 1997-66224P 19971120
 AB WO 9926476 A UPAB: 20010418

NOVELTY - Psoralen compounds and their salts are new.

DETAILED DESCRIPTION - Psoralen compounds comprise substituent A on the pyrone ring chosen from $(CH_2)_u-NH_2$, $(CH_2)_w-J-(CH_2)_z-NH_2$, $(CH_2)_w-J-(CH_2)_x-K'-(CH_2)_z-NH_2$, $(CH_2)_w-J-(CH_2)_x-K'-(CH_2)_y-L-(CH_2)_z-NH_2$; J, K', L = O or NH;
 $u = 1-10$;
 $w = 1-5$;
 $x, y = 2-5$; and
 $z = 2-6$;
 and substituents B, R3, R4, R5 and R6 on the pyrone ring, 5-, 4', 5'- and 8- C atoms, respectively (sic); chosen from H or $(CH_2)_v-CH_3$;
 $v = 0-5$.

An INDEPENDENT CLAIM is also included for inactivating pathogens in biological compositions comprising:

(a) providing, in any order, a compound chosen from primary amino-pyrone-linked psoralens and primary amino-benzene-linked psoralens, photoactivating means for photoactivating the compounds and biological composition suspected of being contaminated with a pathogen containing a nucleic acid;

(b) adding the compound to the biological composition; and
 (c) photoactivating the compound to inactivate the pathogen.

ACTIVITY - Antimicrobial; anti-proliferative.

Small aliquots of three test compounds were added to stock HIV-1 to a compound concentration of 32 nM in 0.5 ml. The stock HIV-1 (105-107 plaque-forming units/ml) was in Dulbecco's Modified Eagle Medium (DMEM)/15% fetal bovine serum. The 0.5 ml test aliquots were placed in 24-well polystyrene tissue culture plates and irradiated with 320-400 nm for 1 minute. Controls included HIV-1 stock only, HIV-1 plus ultraviolet (UV)A only and HIV-1 plus highest concentration of each psoralen tested without UVA. Post-irradiation, all samples were stored frozen at -70 deg. C until assayed for infectivity by a microtiter plaque assay. Aliquots for measurement of residual HIV infectivity in the samples were withdrawn and cultured. Residual HIV infectivity was assayed using MT-2 infectivity assay using assay medium containing 85% DMEM (with high glucose concentration) containing streptomycin (100 micro g/ml), penicillin (100 U/ml), gentamicin (50 micro g/ml), amphotericin B (1 micro g/ml), fetal bovine serum (15%) and Polybrene (RTM) (2 micro g/ml). Test and control samples from the inactivation procedure were diluted in a mixture of 50% assay medium and 50% normal human serum. The samples were diluted serially directly in 96-well plates. The plates were mixed on an oscillatory shaker for 30 seconds and incubated at 37 deg. C in a 5% carbon dioxide (CO₂) atmosphere for 1-18 hours. MT-2 cells (0.025 ml; clone alpha -4) were added to each well to give a concentration of 80000 cells/well. After an additional 1 hour of incubation at 37 deg. C in 5% CO₂, 0.075 ml assay medium containing 1.6% SeaPlaque agarose (RTM: agarose) pre-warmed to 38.5 deg. C was added to each well. The plates were kept at 37 deg. C for a few minutes until several pates (sic) had accumulated and then centrifuged in plate carriers at 600 g for 20 minutes. In the centrifuge, cell monolayers formed prior to gelling of the agarose layer. The plates were incubated for 5 days at 37 deg. C in 5% CO₂ and stained by addition of 0.05 ml of 50 micro g/ml propidium iodine in phosphate-buffered saline (pH 7.4) to each well. After 24-48 hours, the orange fluorescence-stained microplaques were visualized by placing the plates on an 8000 micro W/cm² 304 nm UV light box. The plaques were counted at a magnification of x20 to x25 through a stereomicroscope. The log kill (log titer) of cell-free HIV with 1 minute irradiation with test compound at 32 micro M was 1.9 (5.3) for 3-aminomethyl-4,4,8-trimethylpsoralen hydrochloride, 3.5 (5.5) for 3-aminomethyl-4,4',5',8-tetramethylpsoralen and 1.1 (5.4) for 8-aminomethyl-4,4',5-trimethylpsoralen. The results confirm the compounds are effective in inactivating HIV with levels of inactivation comparable to those observed for AMT.

MECHANISM OF ACTION - Base pair intercalation; nucleic acid photoreactivity.

USE - Used to inactivate pathogens in biological compositions (claimed) and health-related products both in vivo and in vitro, particularly in blood products (plasma, platelet preparations, red-blood cells, packed red-blood cells, serum), blood, cerebrospinal fluid, saliva, urine, feces, semen, sweat, milk, tissue, tissue samples and homogenized tissue samples, and synthetic materials incorporating substances with origin in biological organism including vaccine preparations of alum and pathogen, cell-culture medium, cell cultures and viral cultures. Used for nucleic acid **probe** preparations, to prepare **conjugates** (with acridines, lexitropsins, **proteins** e.g. antibodies or receptor **ligands**, nucleic acids, small molecules useful in diagnostics e.g. fluorescent **probes** and biotin, and material surfaces), to inhibit cell proliferation, to inactivate virus for vaccine preparation and to inactivate pathogens in blood products. Used to provide new routes for synthesizing amino-psoralens and intermediates used to provide psoralens **conjugated** to other **functional groups**. Used in vivo (autologous or homologous reintroduction of human blood), in vitro (analysis of component of blood sample using laboratory equipment) and ex vivo (removal of blood from human and introduction of compound into blood to inactivate pathogens). Used to inactive nucleic-acid containing materials such as lymphocytes (to control

proliferation to prevent graft-versus-host disease in bone marrow transplants and inhibit smooth muscle cells to control proliferation after injury e.g. to prevent restenosis after balloon angioplasty), tissue cells and solutions containing nucleic acids e.g. solutions amplified by polymerase-chain reaction. Used to inactivate viruses including adenoviruses (adenovirus 2, canine hepatitis), arenaviruses (Pichinde, Lassa), bunyaviruses (Turlock, California encephalitis), herpesviruses (Herpes simplex 1 and 2, Cytomegalovirus, Pseudorabies), orthomyxoviruses (influenza), papovaviruses (SV-40), paramyxoviruses (measles, mumps, parainfluenza 2 and 3), picornaviruses during virus growth (poliovirus 1 and 2, Coxsackie A-9, Echo 11), poxviruses (vaccinia, fowl pox), reoviruses (reovirus 2, blue tongue, Colorado tick fever), retroviruses (HIV, avian sarcoma, murine sarcoma, murine leukemia), rhabdoviruses (vesicular stomatitis virus), togaviruses (Western equine encephalitis, Dengue 2 and 4, St. Louis encephalitis), hepadnaviruses (hepatitis B), bacteriophages (lambda, T2), and rickettsiaviruses (Rickettsia akari (rickettsiapox)).

ADVANTAGE - Have enhanced ability to inactivate pathogens in the presence of UV light. Are capable of binding to nucleic acid of pathogens. Provide means of inactivating pathogens whilst potentially retaining suitability of product for intended use.

Dwg.0/0

L27 ANSWER 24 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1998-560723 [48] WPIDS
 DNN N1998-437148 DNC C1998-167998
 TI Detecting gene of in vivo **target protein** of drug - comprises binding in vivo administered drug with antigenic substance via chemical crosslinker to give **probe** and directly **screening** gene of **protein** binding with **probe**.
 DC B03 B04 D16 S03
 IN HIDAKA, H; TANAKA, H
 PA (HIDA-I) HIDAKA H
 CYC 22
 PI JP 10248571 A 19980922 (199848)* 4p
 WO 9953094 A1 19991021 (199952) JA
 RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 W: CA US
 EP 1072688 A1 20010131 (200108) EN
 R: AT BE CH DE ES FR GB IT LI NL SE
 ADT JP 10248571 A JP 1997-54661 19970310; WO 9953094 A1 WO 1998-JP1712
 19980415; EP 1072688 A1 EP 1998-914021 19980415, WO 1998-JP1712 19980415
 FDT EP 1072688 A1 Based on WO 9953094
 PRAI JP 1997-54661 19970310; WO 1998-JP1712 19980415; EP 1998-914021
 19980415
 AB JP 10248571 A UPAB: 19981203
 Detecting a gene of an in vivo **target protein** of a drug comprises binding an in vivo administered drug with an antigenic substance via a chemical crosslinker to give a **probe** and directly **screening** a gene of a **protein** binding with the **probe** using a cDNA expression library containing the administered in vivo gene.

The antigenic substance preferably comprises serum albumin or fluorescein isothiocyanate. The cDNA expression library uses a phage as a vector. The drug comprises non-**protein** substance without intrinsic antigenicity. A drug having no antigenicity or non-**protein** substance is bound with an antigenic substance via a chemical crosslinker e.g. a **group** crosslinking **functional groups** of the drug and antigenic substance including glutaraldehyde, hexamethylene diisothiocyanate, N,N'-ethylene bismaleimide and bisdiazo benzidine to give a **probe** by stirring at room temperature in a solvent. The **probe** is used to directly **screen** a gene of **protein** binding with the **probe**.

ADVANTAGE - Direct and simple detection of a gene of a **target molecule** of a drug is effected without using a drug immobilising column. The method can identify a cellular factor such as a small amount of intranuclear transcription factor.

Dwg.0/0

L27 ANSWER 25 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1998-260961 [23] WPIDS
 DNN N1998-205775 DNC C1998-080951
 TI Synthesis of combinatorial libraries, notably of macrocyclic compounds, e.g., cyclophane(s) - by protection and reaction at specific nitrogen atoms, uses include diagnosis, therapy, and as agrochemicals.
 DC B04 B05 D16 S03
 IN COOK, P D
 PA (ISIS-N) ISIS PHARM INC
 CYC 78
 PI WO 9810286 A1 19980312 (199823)* EN 166p
 RW: AT BE CH DE DK EA ES FI FR GB GH GR IE IT KE LS LU MC MW NL OA PT
 SD SE SZ UG ZW
 W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE
 GH HU IL IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW
 MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN
 YU ZW
 AU 9742480 A 19980326 (199832)
 ADT WO 9810286 A1 WO 1997-US15493 19970904; AU 9742480 A AU 1997-42480
 19970904
 FDT AU 9742480 A Based on WO 9810286
 PRAI US 1996-709160 19960906
 AB WO 9810286 A UPAB: 19980610
 A claimed combinatorial synthetic process comprises: (a) providing a first compound having **functional groups** F1 and F2; (b) placing a blocking group on F1; (c) reacting F2 with a first reagent pool (P1), containing at least 4 different reagents, to form a first mixture of adducts bonded covalently between F2 and the compounds of P1; (d) deblocking F1, to form a first mixture of deblocked compounds; and (e) reacting at least a portion with a second compound, to form a mixture of products bound covalently also at F1.
 USE - The invention relates particularly to macrocyclic compounds, notably cyclophanes, macrocycles interrupted by small ring systems to provide two bridgehead atoms, connected to nitrogenous moieties. The nitrogenous sites can be derivatised singly to provide more diversity of compounds, and the technique above, using two sites F1 and F2, can be extended to cover further reactive groups, e.g., F3 and F4, by similar specific blocking, reacting, deblocking, and reacting the freed group cycles. Compounds of these types can have preorganised geometry which matches **target proteins, enzymes, nucleic acids, lipids, and other biological materials**. The combinatorial approach enables libraries of related compounds for **screening** for **biological activities** to be constructed rapidly. The **screening** may reveal compounds which are inhibitors of pathogens, e.g., viruses, mycobacteria, gram negative and gram positive bacteria, protozoa, and parasites; inhibitors of ligand-receptor interactions, e.g., PDGF (platelet derived growth factor), LTB4 (leucotriene B4), IL-6, and complement C5A; of transcription factors, e.g., p50 (NFkB protein) and fos/jun; of PLA-2 (phospholipase-A2); and of cell-based interactions, e.g. ICAM induction. The libraries can also be **screened** for diagnostic reagents, including those for the above therapeutic systems, or as assay and **probe** reagents. A third area is as metal chelators and contrast agent nuclei; and a fourth as agrochemicals, e.g., as herbicides and insecticides.
 ADVANTAGE - The economies of time and labour possible by synthesis of

libraries of compounds for screening rather than individual compounds are well known.

Dwg.0/15

L27 ANSWER 26 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1997-384662 [35] WPIDS
 CR 1983-736619 [33]; 1994-365411 [45]; 1996-332642 [33]; 1997-144407 [12];
 1997-144862 [13]; 1997-178398 [16]
 DNN N1997-320292 DNC C1997-123264
 TI New release tag compound used as analytical labelling agent - comprising reactivity group, linking group and signal group forming detectable volatile compound on cleavage.
 DC B04 B05 D16 S03
 IN ABDEL-BAKY, S; ALLAM, K; GIESE, R W
 PA (UYNE-N) UNIV NORTHEASTERN
 CYC 1
 PI US 5650270 A 19970722 (199735)* 38p
 ADT US 5650270 A Cont of US 1982-344394 19820201, CIP of US 1987-45089
 19870504, US 1990-496251 19900320
 FDT US 5650270 A Cont of US 4709016
 PRAI US 1990-496251 19900320; US 1982-344394 19820201; US 1987-45089
 19870504
 AB US 5650270 A UPAB: 19970828

A novel release tag compound, for labelling substances for analytical purposes, is of formula Sg-CO-L-Rx (I). L (linking group) = O or NH; Rx (reactivity group) = phenylene connected to a reactive **functional group**; Sg (signal group) = 1-20C, C-bonded organic moiety selected from alkyl, ketoalkyl, alkenyl and alkynyl, where alkyl, ketoalkyl and alkyl are substituted by at least 2 electronegative groups E and alkynyl is substituted by at least one group E; E= halo, CN, dihalomethyl or trihalomethyl; provided that (i) if Sg = ketoalkyl, alkenyl or alkynyl, then Sg contains at least one moiety selected from beta -E-alkynyl, alpha -E-alkynyl, beta -E-keto, alpha -E-alkenyl and alpha -E- alpha -alkenyl (where the alpha -position is the carbon adjacent to the CO of -CO-L-Rx), (ii) if Sg = alkyl, the alpha -carbon bears at least 2 electronegative substituents but not more than one F and (iii) on cleavage of (I) at the COL portion, Sg is released in a volatile form suitable for electron capture de termination in the gas phase.

USE - Compounds labelled with (I) release a signal group in the form of a readily detectable volatile compound at a desired point in an analytical procedure. Typically (I) are used for labelling **proteins** (e.g. hormones, **enzymes**, antigens, antibodies, receptors or transport **proteins**), peptides, aminoacids, polynucleotides (e.g. genes, gene fragments and DNA **probes**), nucleotides, nucleosides, nucleobases, lipids, carbohydrates, drugs, cells, viruses, vitamins, coenzymes, **bioactive** amines, aflatoxins, polyaromatic hydrocarbons and pesticides. The labelled products may be used in analytical procedures such as the human genome project, testing for infectious diseases (e.g. AIDS) and genetic screening.

ADVANTAGE - By using different release tags, a large number of analytes in a sample can be determined simultaneously. Reactivity groups Rx can be varied to bond specifically and selectively to particular substances to be labelled, and cleavage can be carried out under particular desired conditions. The analytical method using the release tags is sensitive and widely applicable.

Dwg.0/2

L27 ANSWER 27 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1995-320308 [41] WPIDS
 DNC C1995-142254
 TI Adding peptide nucleic acid units to resin bound oligomer - using sub-monomer, or complete preformed monomer, synthon(s), used to construct

random or predefined sequences for screening for potential pharmaceuticals, also new amino acid-peptide nucleic acid chimaeras.

DC B04 D16
 IN COOK, P D; KIELY, J; SPRANKLE, K
 PA (ISIS-N) ISIS PHARM INC
 CYC 60
 PI WO 9523163 A1 19950831 (199541)* EN 103p
 RW: AT BE CH DE DK ES FR GB GR IE IT KE LU MC MW NL OA PT SD SE SZ UG
 W: AM AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KE KG KP
 KR KZ LK LT LU LV MD MG MN MW MX NL NO NZ PL PT RO RU SD SE SI SK
 TJ TT UA US UZ VN
 AU 9519261 A 19950911 (199550)
 US 5539083 A 19960723 (199635) 38p
 JP 09503523 W 19970408 (199724) 104p
 EP 777678 A1 19970611 (199728) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 AU 684152 B 19971204 (199806)
 EP 777678 A4 19970716 (199813)
 US 5831014 A 19981103 (199851)
 US 5864010 A 19990126 (199911)
 JP 11209393 A 19990803 (199941) 39p
 EP 777678 B1 19991013 (199947) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 DE 69512794 E 19991118 (200001)
 US 6204326 B1 20010320 (200118)
 CA 2183371 C 20010403 (200124) EN
 ADT WO 9523163 A1 WO 1995-US2182 19950222; AU 9519261 A AU 1995-19261
 19950222; US 5539083 A US 1994-200742 19940223; JP 09503523 W JP
 1995-522421 19950222, WO 1995-US2182 19950222; EP 777678 A1 EP 1995-911848
 19950222, WO 1995-US2182 19950222; AU 684152 B AU 1995-19261 19950222; EP
 777678 A4 EP 1995-911848 19950222; US 5831014 A CIP of US 1994-200742
 19940223, WO 1995-US2182 19950222, US 1996-693144 19960813; US 5864010 A
 Div ex US 1994-200742 19940223, US 1996-587648 19960117; JP 11209393 A Div
 ex JP 1995-522421 19950222, JP 1998-322576 19950222; EP 777678 B1 EP
 1995-911848 19950222, WO 1995-US2182 19950222; DE 69512794 E DE
 1995-612794 19950222, EP 1995-911848 19950222, WO 1995-US2182 19950222; US
 6204326 B1 CIP of US 1994-200742 19940223, Cont of WO 1995-US2182
 19950222, Cont of US 1996-693144 19960813, US 1998-131270 19980807; CA
 2183371 C CA 1995-2183371 19950222, WO 1995-US2182 19950222
 FDT AU 9519261 A Based on WO 9523163; JP 09503523 W Based on WO 9523163; EP
 777678 A1 Based on WO 9523163; AU 684152 B Previous Publ. AU 9519261,
 Based on WO 9523163; US 5831014 A CIP of US 5539083, Based on WO 9523163;
 US 5864010 A Div ex US 5539083; EP 777678 B1 Based on WO 9523163; DE
 69512794 E Based on EP 777678, Based on WO 9523163; US 6204326 B1 CIP of
 US 5539083, Cont of US 5831014; CA 2183371 C Based on WO 9523163
 PRAI US 1994-200742 19940223; US 1996-693144 19960813; US 1996-587648
 19960117; US 1998-131270 19980807
 AB WO 9523163 A UPAB: 19991122
 Additional peptide nucleic acid (PNA) units are added to an
 amino-terminated PNA oligomer (A) on a solid phase synthesis resin by: (1)
 reacting terminal NH₂ in (A) with one reactive gp. in a bifunctional
 acetyl synthon (I); (2) reacting the prod. with an alkyldiamine synthon
 (II) in which one NH₂ is protected and the other free so that the reactant
 gp. in (I) reacts with free NH₂, forming a resin bound extended oligomer
 in which the extension contains sec. and protected amino gps.; (3)
 treating the prod. with an acetylnucleobase synthon (III) to form an amide
 bond between the sec. amino, producing a new protected, amino-terminated
 oligomer; (4) deprotecting the terminal gp., and (5) repeating steps (1) -
 (4) as often as required. In modifications: (a), to add random PNA units,
 a mixt. of different (III) is used in step (2) or the prod. of step (2) is
 divided into portions, reacted with individual (III) and then the portions
 mixed; (b) the starting oligomer is an NH₂-terminated amino acid oligomer;
 (c) the method is used to produce mixed PNA-amino acid oligomers; (d) (II)

and (III) are replaced (in any modification) by a single alkyldiamine-acetylnucleobase synthon (IV); (e) in any modification, (A) is replaced by a 1-(2-carbonylmethylnucleobase)-3-oxo-morpholine synthon (V) to form a N-(2-(nucleobase)acetyl)-N-(hydroxyethyl)glycine end gp., and this converted to corresp. N-(aminoethyl)glycine gp., before the next reaction cycle; if, to add random PNA, (A) is reacted with PNA synthons contg. different nucleobases (opt. after division into portions); (g) an activated resin phase is reacted with a monoprotected diamine synthon (VI), deprotected, reacted sequentially with 2-haloacetate ester (VII) and 1-acetylnucleobase, deprotected to give a prod. with free COOH and covalently bound acetylnucleobase, then reacted with (VI). Also new are the cpds.: $(AA)^w - ((PNA)^u - (AA)^v)^x (PNA)^y - (AA)^z$ (VIII), where each AA and PNA are, respectively, same or different amino acid and peptide nucleic acid residues; u,v,x and y = 1-500; w and z = 0-500; the total of u,v,w,x,y and z is <500 (esp. <25).

USE - The methods are used to produce combinatorial libraries of oligomeric PNA (or PNA-amino acid chimaeras) with random or (partially) predefined sequences, useful for **screening** for cpds. with ability to bind to **proteins** and/or nucleic acids. Partic. the prods. are (1) **enzyme** inhibitors, partic. of phospholipase A2 for treating inflammatory disease (e.g. atopic dermatitis and bowel disease); (2) gene modulators; (3) diagnostic reagents (they hybridise specifically to nucleic acids involved in disease) and (4) primers and probes for studying **enzyme** biochemistry and **protein/nucleic acid interaction**.

ADVANTAGE - By using submonomer units in the synthesis, a non-regular backbone can be produced, providing greater diversity (e.g. Pro residues can be introduced to generate sec. structure). Some submonomers need be prep'd. only once (in large quantity); they may be reactive enough to obviate need for coupling agents, and less complex nucleotide synthons are required. PNA have higher binding affinity for nucleic acid than the complementary nucleic acid.

Dwg.0/8

L27 ANSWER 28 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1995-074930 [10] WPIDS
 DNC C1995-033297
 TI Prepn. of arrays of similar cpds. for biological **screening** - using multi-component combinational synthesis in n-dimensional array, each having a position for each combination.
 DC A96 B04 B05 J04
 IN ARMSTRONG, R W
 PA (REGC) UNIV CALIFORNIA; (ONTO-N) ONTOGEN CORP
 CYC 54
 PI WO 9502566 A1 19950126 (199510)* EN 91p
 RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE
 W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ
 LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US
 UZ VN
 AU 9473673 A 19950213 (199519)
 EP 708751 A1 19960501 (199622) EN
 R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
 JP 09506857 W 19970708 (199737) 80p
 ADT WO 9502566 A1 WO 1994-US8141 19940715; AU 9473673 A AU 1994-73673
 19940715; EP 708751 A1 EP 1994-922629 19940715, WO 1994-US8141 19940715;
 JP 09506857 W WO 1994-US8141 19940715, JP 1995-504767 19940715
 FDT AU 9473673 A Based on WO 9502566; EP 708751 A1 Based on WO 9502566; JP
 09506857 W Based on WO 9502566
 PRAI US 1994-180863 19940113; US 1993-92862 19930716
 AB WO 9502566 A UPAB: 19970723
 An array of cpds. having a common core structure (CCC) comprising the prods. of a multiple component combinatorial array synthesis (MCCA) having at least 3 components. The components of the MCCA comprise: (a) a 1st gp.

of reactants having a same 1st functional gp.; (b) a 2nd gp. of reactants having a same 2nd functional gp.; and (c) a 3rd gp. of reactants, having a same 3rd functional gp.; in which the functional gps. of (a), (b), and (c) react with each other to form the CCC. Also claimed are: (A) making a combinatorial array of cpds. having a CCC using an n component combinatorial array synthesis, where n corresponds to the no. of reaction components, n being at least 3, where each component comprises a gp. of reactants having the same functional gp.; the method comprises: (a) organising a series of reaction vessels in an n dimensional array where each reaction vessel is identifiable by its coordinates in the array, each axis corresp. to a different component and each position corresp. to a different reactant; (b) adding the reactants of the n components to the n dimensional array of reaction vessels so that the reactant is added to all of the reaction vessels corresp. to that reactant; and (c) reacting the contents to form the cpds. of the array; (B) creating a CA of cpds. with a CCC comprising: (a) identifying the desired core structure; (b) identifying a MCCA reaction capable of generating the core structure; (c) preparing an opt. combinatorial array of cpds. using the identified MCCA reaction as in (B); (C) conducting in vitro binding studies on a biological material comprising: (a) adding the biological material to an array of compounds, each cpd. in the array having a CCC and being bound to a solid support; and (b) measuring the binding of each cpd. to the biological material; and (D) a linker bound to a polymer, useful for binding cpds. in solid phase synthesis, and having a formula of type (I): (POLYMER)-NHCOCH₂CH₂CH(CH₂CH₂N₃)COOH (I).

USE - The method allows generation of numerous organic cpds. to form an array or library to **probe** structure-activity relationships for the development of new therapeutic agents in a simple, rapid, and efficient manner. Many **biologically active** molecules possess one of a relatively small gp. of core structures, and by appropriate modification, a library, or sub-library, can be built up. Opt. automation techniques analogous to those used in nucleotide and peptide synthesis can be used, with the same reactant added to all the compartments in the same row, column or layer. A wide range of chemical reactions (including soln., solid phase, photochemical, electrochemical, free radical, or **enzymatic**) can be used in prepn. of the CCC. For solid state bound cpds., which can be freed from reactants and impurities more easily, it is possible, after cleavage to conduct in vitro bioassays directly e.g. by binding to biological material. Only a small amt. of material is required for a **screen**, making isolation and purificn. unnecessary in a first investigation.

ADVANTAGE - Much time and labour can be saved by the new approach. Rather than individual, usually linear, syntheses for each cpd., the method produces a CCC on a geometric scale as a prod. of the no. of reaction vessels, e.g. 5 x 5 x 5 gives 125 analogues. The MCCA technique should therefore accelerate new drug development and make research **screening** more widely available. **Screening** the cpds. is simultaneous, and cpds. are identified by their position in the matrix.

Dwg.6/11

L27 ANSWER 29 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD
 AN 1989-278393 [38] WPIDS
 DNN N1989-212563 DNC C1989-123269
 TI New bis heterocyclic chelating agents - and lanthanide chelates for multi-label spectro-fluorometric assays.
 DC B03 B04 J04 S03
 IN KWIATKOWSK, M; MUKKALA, V
 PA (WALL-N) WALLAC OY
 CYC 12
 PI WO 8908263 A 19890908 (198938)* EN 71p
 RW: AT BE CH DE FR GB IT LU NL SE
 W: JP US

ADT WO 8908263 A WO 1989-SE73 19890222

PRAI SE 1988-613 19880223

AB WO 8908263 A UPAB: 19951114

Chelating agents of formula (I) and their acid, ester, salt and chelate forms are new: A1-A6 = N or CR; n = 0-2; R = H or C-, O- and/or N-contg. gps. (same or different); Z and A1 = gps. contg. at least one heteroatom with a free pair of electrons, capable of chelating a metal ion together with the ring N atoms; B = a bridging gp. allowing (a) electron delocalisation between the two rings and (b) simultaneous coordination of the two ring N atoms with a chelated metal ion to form a 5- or 6-membered ring; X = an inert and stable bridging gp. with an aliphatic C atom separating Y from one of the rings; Y = a functional gp. or the residue of an organic cpd.; provided that for chelates of metals other than lanthanides, at least one R is other than H when n = 0, Z = Z1 = N(CH₂COO⁻)₂ and all A1-A6 = CR.

USES - (I) may be used as probes or labels in homogeneous or heterogeneous immunoassays or nucleic acid hybridization assays, nuclei acid sequencing, fluorescence microscopy, cytometry and nuclei acid or protein finger printing.

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Dwg.0/0

L27 ANSWER 30 OF 30 WPIDS COPYRIGHT 2002 DERWENT INFORMATION LTD

AN 1989-208565 [29] WPIDS

DNC C1989-092531

TI Methods appts. and compsns. for ligating ligands - by binding to common target to bring reactive gps. into reactive position, used esp. with polynucleotide probes.

DC A96 B02 B04 C03 D16

IN CRUICKSHAN, K A; MORRISON, L E; ROYER, G P; CRUICKSHANK, K A

PA (VYSI-N) VYSIS INC; (STAD) AMOCO CORP; (REGC) UNIV CALIFORNIA

CYC 15

PI EP 324616 A 19890719 (198929)* EN 29p

R: AT BE CH DE FR GB IT LI LU NL SE

AU 8928485 A 19890727 (198937)

JP 02005898 A 19900110 (199008)

US 5219734 A 19930615 (199325) 22p

EP 324616 B1 19950329 (199517) EN 34p

R: AT BE CH DE FR GB IT LI LU NL SE

DE 68921901 E 19950504 (199523)

US 5449602 A 19950912 (199542) 23p

CA 1339304 C 19970819 (199747)

US 5686243 A 19971111 (199751) 21p

JP 2858771 B2 19990217 (199912) 26p

US 6306587 B1 20011023 (200165)

ADT EP 324616 A EP 1989-300258 19890112; JP 02005898 A JP 1989-7525 19890113;

US 5219734 A US 1988-143586 19880113; EP 324616 B1 EP 1989-300258

19890112; DE 68921901 E DE 1989-621901 19890112, EP 1989-300258 19890112;

US 5449602 A US 1988-143586 19880113; CA 1339304 C CA 1988-586425

19881220; US 5686243 A Cont of US 1988-143586 19880113, US 1995-436117

19950508; JP 2858771 B2 JP 1989-7525 19890113; US 6306587 B1 Div ex US

1988-143586 19880113, Div ex US 1995-436117 19950508, US 1997-967011

19971110

FDT DE 68921901 E Based on EP 324616; US 5686243 A Cont of US 5449602; JP 2858771 B2 Previous Publ. JP 02005898; US 6306587 B1 Div ex US 5449602, Div ex US 5686243

PRAI US 1988-143586 19880113; US 1995-436117 19950508; US 1997-967011 19971110

AB EP 324616 A UPAB: 19930923

Compsn useful for forming dimers on photoactivation comprises a coumarin of formula (I) where R₃, R₅ = OH or OMe; and R₁, R₂, R₄, R₆ = H, reactive gp capable of reacting with aliphatic amines, a ligand, or antiligand. Compsn is claimed comprising a polynucleotide having at least

one photoreactive **functional gp** at or about the 3' or 5' termini, chosen from coumarins, psoralens, anthracenes, pyrenes, carotenes, tropones, chromones, quinones, maleic anhydride, alkyl maleimide, olefins, ketones, azides, polyolefins characterised by **conjugated** double bonds and ketone functionality and derivs.

Polynucleotide is characterised by the 3' terminal of one strand bonded to the 5' terminal of a second strand through a dimer formed from reactive functional gps, pref photoreactive gps. Method for ligating **ligands** which bind to a common target comprises (a) contacting a target with a first **ligand** and a second **ligand**, where at least one of the **ligands** has a reactive **functional gp**. (A) capable of forming a covalent bond between the first and second **ligands** on activation when the **ligands** are placed in a reactive position, and the first and second **ligands** are capable of simultaneously binding to the target in a reactive position to form a target-first-second **ligand** complex; and (b) activating the reactive **functional gp** to form a covalent bond between the **ligands** while in reactive position.

USE/ADVANTAGE - Used in DNA and RNA hybridisation assays in diagnosis of physiological or pathological conditions or bacterial or viral infections in humans, animals or plants, and in detection of bacterial contamination of foodstuffs or identification of specific genes in bacterial cultures to detect eg antibiotic resistance.

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Tran 09/738,954

=> fil hcaplus

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FILE COVERS 1907 - 18 Mar 2002 VOL 136 ISS 12
FILE LAST UPDATED: 15 Mar 2002 (20020315/ED)

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CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the CAS files between 12/27/01 and 1/23/02. As of 1/23/02, the situation has been resolved. Searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator executed between 12/27/01 and 1/23/02 may be incomplete. See the NEWS message on this topic for more information.
'OBI' IS DEFAULT SEARCH FIELD FOR 'HCAPLUS' FILE

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(FILE 'MEDLINE' ENTERED AT 11:09:22 ON 18 MAR 2002)
DEL HIS Y

FILE 'HCAPLUS' ENTERED AT 11:11:57 ON 18 MAR 2002

E PROTEOME/CT
E E3+ALL
L1 1523 S PROTEOM?
L2 66917 S PROBE#
L3 64397 S SCREEN?
L4 178337 S BIOACTIV? OR BIO? (L) ACTIVIT?
L5 25 S L1 AND L2
L6 5 S L5 AND (L3 OR L4)
L7 4092 S TARGET (L) (PROTEIN# OR ENZYME#)
L8 122 S L2 AND L7
L9 114290 S LIGAND#
L10 17 S L9 AND L8
L11 5236 S L7 OR TARGET (L) (MOL# OR MOLE?)
L12 122 S L11 AND L8
L13 184 S L2 AND L11
L14 26 S L13 AND L9
L15 26 S L14 OR L10

Tran 09/738,954

L16 18091 S FUNCTIONAL (3A) (GROUP# OR GRP#)
L17 9 S L16 AND L13
L18 861 S L2 (L) ACTIVIT?
L19 4 S L18 AND L1
L20 4 S L18 AND L11
L21 37 S L15 OR L17 OR L19 OR L20
L22 24 S L21 AND (L1 OR PROTEIN#)
L23 15 S L21 AND ENZYM?
L24 28 S L22 OR L23

FILE 'HCAPLUS' ENTERED AT 11:21:01 ON 18 MAR 2002

=> d .ca 124 1-28

L24 ANSWER 1 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:90063 HCAPLUS
DOCUMENT NUMBER: 136:163716
TITLE: Labeled peptides, proteins and antibodies
and processes and intermediates useful for their
preparation
INVENTOR(S): Hahn, Klaus M.; Toutchkine, Alexei; Muthyala, Rajeev;
Kraynov, Vadim; Bark, Steven J.; Burton, Dennis R.;
Chamberlain, Chester
PATENT ASSIGNEE(S): The Scripps Research Institute, USA
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008245	A2	20020131	WO 2001-US22194	20010713
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-218113	P 20000713
			WO 2000-US26821	W 20000929
			US 2001-279302	P 20010328
			US 2001-839577	A 20010420

OTHER SOURCE(S): MARPAT 136:163716
AB The invention provides peptide synthons having protected functional groups
for attachment of desired moieties (e.g. functional mols. or probes).
Also provided are peptide conjugates prep'd. from such synthons, and
synthon and conjugate prepn. methods including procedures for identifying
optimum probe attachment sites. Biosensors are provided having functional
mols. that can locate and bind to specific biomols. within living cells.
Biosensors can detect chem. and physiol. changes in those biomols. as
living cells are moving, metabolizing and reacting to its environment.
Methods are included for detecting GTP activation of a Rho GTPase protein
using polypeptide biosensors. When the biosensor binds GTP-activated Rho
GTPase protein, an environmentally sensitive dye emits a signal of a
different lifetime, intensity or wavelength than when not bound. New

fluorophores whose fluorescence responds to environmental changes are also provided that have improved detection and attachment properties, and that can be used in living cells, or in vitro.

- IC ICM C07K001-00
CC 9-14 (Biochemical Methods)
Section cross-reference(s): 7, 15, 34, 41
ST labeled peptide **protein** antibody prep; biosensor targeting biomol living cell **probe**; GTP activation Rho GTPase detection polypeptide biosensor; fluorophore fluorescence **probe** environmental change living cell
IT Animal cell line
(3T3; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Imaging
(FLAIR (fluorescent activation indicator for Rho **proteins**); labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Transcription factors
RL: PRP (Properties)
(GCN4, peptide tag derived from leucine zipper of; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Histocompatibility antigens
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(HLA-B27, fusion **proteins** with GFP; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Immunoglobulin receptors
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(IgE type I; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Resins
RL: RCT (Reactant); RACT (Reactant or reagent)
(MBHA; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Histocompatibility antigens
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(MHC (major histocompatibility complex); labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Phycoerythrins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(P; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Phycoerythrins
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(R-phycoerythrins, conjugates with peptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Imaging
(Rac activation in cells; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)
IT Wound healing

(Rac role in; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(WASP (Wiskott-Aldrich syndrome **protein**), polypeptide biosensor as peptide of, binding to cdc42; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Functional groups**

(aminoxy, peptide contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Neutrophil**

(assay of cdc42 activity in cell lysates of stimulated; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Physics**

(biophysics, **probes**; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(cellular, localization in living cells; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Allophycocyanins**

Phycoerythrins

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(conjugates with peptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Alexa**

Drugs

(conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Antibodies**

Peptides, biological studies

Polynucleotides

Proteins

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(conjugates; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(cyan fluorescent **protein**, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Fluorescent dyes**

(cyanine, conjugates with peptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Gene**

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified);

BUU (Biological use, unclassified); BIOL (Biological study); PREP (Preparation); USES (Uses)

(encoding fusion **proteins**; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(enhanced green fluorescent **protein**, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(enhanced yellow green fluorescent **protein**, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Resonant energy transfer

(fluorescence; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Cyanine dyes

(fluorescent, conjugates with peptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Fluorescent substances

(fluorophores, for detecting changes in responses of living cells to environment; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Immunoglobulins

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(fragments, conjugates; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Rho **protein** (G **protein**)

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(fusion **proteins** with fluorescent **proteins**; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT G **proteins** (guanine nucleotide-binding **proteins**)

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation)

(gene CDC42; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT G **proteins** (guanine nucleotide-binding **proteins**)

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)

(gene rac, polypeptide biosensor as p21-activated kinase peptide binding to; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT **Proteins**

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU

(Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(green fluorescent, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Nucleic acids

RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(indicators for, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Biosensors

Blood serum

Cell

Cell migration

Endoplasmic reticulum

Fibroblast

Fluorescence

Fluorescence excitation

Fluorescent dyes

Genetic vectors

Human

Phosphorescence

Phosphorescent substances

Signal transduction, biological

Stress, animal

Stress, microbial

Stress, plant

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Actins

Calmodulins

Myosins

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Peptides, biological studies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT DNA

Proteins

RNA

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Antibodies

Antigens

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT Platelet-derived growth factors

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Nucleic acids

RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(labeled; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Antibodies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(labeled; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Peptides, biological studies

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(labeled; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT **Proteins**

RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(labeled; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Protein motifs

(leucine zipper, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Fusion **proteins** (chimeric **proteins**)

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)

(of Rho GTPase **protein** and fluorescent **proteins**; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Affinity

(of peptide conjugate for **target**; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Rho **protein** (G **protein**)

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)

(p21rhoA; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Actins

RL: BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent)

(polymn., Rac1 activation localization at site of; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT Ligands

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(polypeptide-dye conjugates sensitive to binding by; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

- IT pH
(polypeptide-dye conjugates sensitive to; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT ESR (electron spin resonance)
(probes, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT **Protein** motifs
(protein-binding domain of p21-activated kinase 1, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Phosphorylation, biological
(protein; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT **Proteins**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(red fluorescent **protein**, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Sensors
(responsive, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Dyes
(sensitive to pH or ligand binding or other, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Cage compounds
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sensors, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Dyes
(solvatochromic, conjugates with polypeptides; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT **Proteins**
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(yellow green fluorescent **protein**, conjugates, polypeptide biosensor contg.; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Actinins
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(.alpha.-; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT Lactoglobulins
RL: RCT (Reactant); RACT (Reactant or reagent)
(.beta.-, labeling with tetramethylrhodamine N-hydroxysuccinimide ester; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)
- IT 144713-51-9, Erk4 **protein** kinase

RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(Erk4 protein kinase; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 9059-32-9DP, GTPase, conjugates with fluorescent proteins
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GTP-activated Rho; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 394257-19-3P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence of peptide tag derived from GCN4 leucine zipper; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 271795-11-0P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence, C-terminal p21 binding domain peptide; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 393511-94-9P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence, N-terminal p21 binding domain peptide; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 394257-16-0
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence, as tag in cellular protein localization; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 394257-20-6P
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(amino acid sequence, cloning and site-specific cysteine mutagenesis of; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 394257-21-7
RL: PRP (Properties)
(amino acid sequence; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 393512-08-8 393512-09-9 393512-10-2 393512-11-3
RL: PRP (Properties)
(as merocyanine dye; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 76-05-1, Trifluoroacetic acid, uses 5961-85-3, Tris(2-carboxyethyl)phosphine
RL: NUU (Other use, unclassified); USES (Uses)
(in eliminating multiply-labeled side products; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)

IT 50-01-1P, Guanidine hydrochloride
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(in improving yield of labeled product; labeled peptides,

- proteins and antibodies and processes and intermediates useful for prepn.)
- IT 9002-07-7, Trypsin 9004-07-3, .alpha.-Chymotrypsin
 RL: NUU (Other use, unclassified); USES (Uses)
 (labeled peptide cleavage with; labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)
- IT 137632-07-6, Erk1 kinase 144713-50-8, Erk3 protein kinase
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)
- IT 137632-08-7, Erk2 kinase
 RL: ANT (Analyte); BSU (Biological study, unclassified); RCT (Reactant); ANST (Analytical study); BIOL (Biological study); RACT (Reactant or reagent)
 (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)
- IT 394257-19-3DP, tetramethylrhodamine-labeled
 RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (labeled peptides, proteins and antibodies and processes and intermediates useful for prepn.)
- IT 65-61-2DP, Acridine Orange, conjugates with peptides 1239-45-8DP,
 Ethidium Bromide, conjugates with peptides 1325-87-7DP, Cascade Blue,
 conjugates with peptides 1461-15-0DP, Calcein, conjugates with peptides 2321-07-5DP, Fluorescein, conjugates with peptides 2768-89-0DP,
 Rhodamine X, conjugates with peptides 3520-42-1DP, Lissamine Rhodamine B, conjugates with peptides 7059-24-7DP, Chromomycin A3, conjugates with peptides 7240-37-1DP, 7-AAD, conjugates with peptides 10199-91-4DP,
 NBD, conjugates with peptides 18378-89-7DP, Mithramycin, conjugates with peptides 23491-45-4DP, Hoechst 33258, conjugates with peptides 23491-52-3DP, Hoechst 33342, conjugates with peptides 25535-16-4DP,
 Propidium Iodide, conjugates with peptides 30230-57-0DP, conjugates with peptides 41085-99-8DP, conjugates with peptides 43070-85-5DP,
 Hydroxycoumarin, conjugates with peptides 47165-04-8DP, DAPI, conjugates with peptides 51908-46-4DP, Dansyl aziridine, conjugates with peptides 70281-37-7DP, Tetramethylrhodamine, conjugates with peptides 76421-73-3DP, Monochlorobimane, conjugates with peptides 76433-29-9DP,
 LDS 751, conjugates with peptides 82354-19-6DP, Texas Red, conjugates with peptides 82446-52-4DP, Lucifer Yellow, conjugates with peptides 96314-96-4DP, Indo-1, conjugates with peptides 96314-98-6DP, Fura-2,
 conjugates with peptides 107091-89-4DP, Thiazole Orange, conjugates with peptides 107347-53-5DP, TRITC, conjugates with peptides 112117-57-4DP,
 conjugates with peptides 123632-39-3DP, Fluo-3, conjugates with peptides 126208-12-6DP, Carboxy-SNARF-1, conjugates with peptides 143245-02-7DP,
 conjugates with peptides 143413-84-7DP, TOTO-1, conjugates with peptides 143413-85-8DP, YOYO-1, conjugates with peptides 146368-15-2DP, Cy5,
 conjugates with peptides 146368-16-3DP, Cy3, conjugates with peptides 149838-22-2DP, FM 1-43, conjugates with peptides 153967-04-5DP, SNARF,
 conjugates with peptides 157199-59-2DP, TO-PRO-1, conjugates with peptides 157199-63-8DP, TO-PRO-3, conjugates with peptides 165599-63-3DP, BODIPY-FL, conjugates with peptides 166196-17-4DP,
 TOTO-3, conjugates with peptides 169799-14-8DP, Cy7, conjugates with peptides 194100-76-0DP, SYTOX Green, conjugates with peptides 204934-16-7DP, BODIPY TR, conjugates with peptides 237752-36-2DP, Red 613, conjugates with peptides 247145-11-5DP, Alexa-532, conjugates with peptides 287384-28-5DP, BODIPY TMR, conjugates with peptides 324767-53-5DP, SYTOX Orange, conjugates with peptides 396076-95-2DP,

TruRed, conjugates with peptides 396077-00-2DP, SYTOX Blue, conjugates with peptides
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 393511-95-0P
 RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); RCT (Reactant); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 56-65-5, ATP, biological studies 86-01-1, GTP 22537-22-0, Magnesium ion, biological studies 142805-58-1, MEK kinase
 RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 393511-96-1DP, ditetramethylrhodamine-labeled 393511-97-2P
 RL: BYP (Byproduct); PRP (Properties); PREP (Preparation)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 64-19-7, Acetic acid, uses 7440-66-6, Zinc, uses
 RL: NUU (Other use, unclassified); USES (Uses)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 271795-07-4P 271795-10-9P 393511-92-7P 393511-93-8P 393511-96-1P
 394257-17-1P 394656-50-9P 394656-72-5P
 RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 393511-93-8DP, tetramethylrhodamine-labeled 394656-50-9DP,
 tetramethylrhodamine-labeled 394679-45-9P
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 1080-74-6, 3-(Dicyanomethylene)indan-1-one 1127-35-1 4229-44-1,
 N-Methylhydroxylamine hydrochloride 5292-43-3 13139-15-6 17576-35-1,
 1,3,3-Trimethoxy propene 27144-18-9 73259-81-1 246256-50-8
 271795-14-3 393512-00-0 393512-07-7 393512-12-4
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 271795-03-0P 271795-04-1P 271795-05-2P 393511-98-3DP, resin-bound
 393511-99-4DP, resin-bound 393512-01-1P 393512-04-4P 394257-18-2P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 393512-02-2P 393512-03-3P 393512-05-5P 393512-06-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (labeled peptides, **proteins** and antibodies and processes and intermediates useful for prep.)

IT 9059-32-9, GTPase
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (of Rho **protein**; labeled peptides, **proteins** and

antibodies and processes and intermediates useful for prepn.)

IT 70-18-8, Glutathione, miscellaneous
 RL: MSC (Miscellaneous)
 (peptide not; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT 177893-51-5P, p21-Activated kinase
 RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (polypeptide biosensor as peptide of, binding to Rac; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT 142243-02-5, MAP kinase
 RL: ANT (Analyte); ARG (Analytical reagent use); BSU (Biological study, unclassified); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (polypeptide biosensor; labeled peptides, **proteins** and antibodies and processes and intermediates useful for prepn.)

IT 394292-00-3 394292-01-4 394292-02-5 394292-03-6 394292-04-7
 394292-05-8 394292-06-9 394292-07-0 394292-08-1
 RL: PRP (Properties)
 (unclaimed nucleotide sequence; labeled peptides, **proteins** and antibodies and processes and intermediates useful for their prepn.)

IT 394291-97-5 394291-98-6 394291-99-7
 RL: PRP (Properties)
 (unclaimed **protein** sequence; labeled peptides, **proteins** and antibodies and processes and intermediates useful for their prepn.)

IT 394211-44-0 394211-45-1
 RL: PRP (Properties)
 (unclaimed sequence; labeled peptides, **proteins** and antibodies and processes and intermediates useful for their prepn.)

L24 ANSWER 2 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:51669 HCAPLUS
 DOCUMENT NUMBER: 136:80846
 TITLE: Dipstick assays with a set of different **probes** to target double-stranded DNA in sample solution
 INVENTOR(S): Lee, Helen; Dineva, Magda Anastassova; Hu, Hsiang Yun
 PATENT ASSIGNEE(S): UK
 SOURCE: PCT Int. Appl., 70 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002004671	A2	20020117	WO 2001-GB3039	20010706
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

GB 2000-16836 A 20000707

- PRIORITY APPLN. INFO.: AB Improved dipstick assays for testing for the presence of a target nucleic acid in a sample soln. are described. A chromatog. dipstick is provided which comprises a contact end for contacting the sample soln. and a capture zone, remote from the contact end, for capturing target nucleic acid. Target nucleic acid in the sample soln. is captured at the capture zone and is detected by a set of labeled oligonucleotides each capable of hybridizing to a different region of the target nucleic acid or these capture probes interact with a hook capture probe bound to the target nucleic acid. The capture probe is coupled to a linker by reaction of a phosphoramidite group attached to the linker with a hydroxyl group of the probe or by reaction of a hydroxyl group of the linker with a phosphoramidite group attached to the probe. A capture probe spacer separates the linker from the capture probe and the present invention demonstrates that longer spacers increase the sensitivity of target nucleic acid detection. The capture probe spacer may be a protein like bovine serum albumin or thyroglobulin. The linker is coupled to the protein by reaction of a primary amino group attached to the linker with a carboxyl group of the protein. Alternatively, a nucleotide can also serve as a capture probe spacer or the capture probe can be coupled to the nucleotide spacer which is then coupled to a protein to space the capture probe from the protein. The non protein is preferably 6 nucleotides in length. Use of the spacer increases the stability of the interaction between the capture probe and the target nucleic acid and improves signal strength. In other methods a plurality of different capture probes are added to the sample soln. which can then be bound by a capture moiety at the capture zone to indirectly capture target nucleic acid. A detection probe capable of hybridizing to the target nucleic acid which can be releasably immobilized to a probe zone between the contact end and capture zone of the the dipstick is another embodiment of the invention. Also, the nucleic acid of interest could be coupled to a plurality of labels or ligands which can be bound by a ligand binding moiety to detect or capture the target nucleic acid when the probe has hybridized to the target nucleic acid. Using this method about 104 copies of Chlamydia trachomatis elementary bodies could be detected in less than an hour including the sample prep. step. Although this assay has a sensitivity of detected about equal to other sandwich hybridization assays, it has the major advantages of speed and simplicity. Kits and dipsticks for carrying out such methods are also described.
- IC ICM C12Q001-68
ICS B01L003-00
- CC 3-1 (Biochemical Genetics)
- ST dipstick assay detection capture target nucleotide sample soln; labeled oligonucleotide **probe** capture target nucleic acid; test kit
dsDNA oligonucleotide **probe** multiple Chlamydia
- IT Dyes
(antibody conjugate; dipstick assays with set of different **probes** to target double-stranded DNA in sample soln.)
- IT Thyroglobulin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(as capture **probe** spacer in capture zone; dipstick assays with set of different **probes** to target double-stranded DNA in sample soln.)
- IT Linking agents
(branches, labels or **ligands** coupled to target nucleic acids using; dipstick assays with set of different **probes** to target double-stranded DNA in sample soln.)
- IT Antibodies
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical

study); BIOL (Biological study); USES (Uses)
(conjugates, with dyes, as capture moiety of dipstick in capture zone;
dipstick assays with set of different **probes** to target
double-stranded DNA in sample soln.)

IT Chlamydia trachomatis
(detection of, nucleic acids of; dipstick assays with set of different
probes to target double-stranded DNA in sample soln.)

IT Immunoassay
(dipstick assays with set of different **probes** to target
double-stranded DNA in sample soln.)

IT Test kits
(dipsticks as, chromatog. strip; dipstick assays with set of different
probes to target double-stranded DNA in sample soln.)

IT DNA
RL: ANT (Analyte); ANST (Analytical study)
(double-stranded; dipstick assays with set of different **probes**
to target double-stranded DNA in sample soln.)

IT Immunoglobulins
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical
study); BIOL (Biological study); USES (Uses)
(fragments, dye conjugates, as capture moiety of dipstick in capture
zone; dipstick assays with set of different **probes** to target
double-stranded DNA in sample soln.)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(immobilized; dipstick assays with set of different **probes** to
target double-stranded DNA in sample soln.)

IT Glass beads
RL: DEV (Device component use); USES (Uses)
(label or detection **ligand** of capture **probe** are
attached to; dipstick assays with set of different **probes** to
target double-stranded DNA in sample soln.)

IT Diagnosis
(mol., of diseases using dipsticks; dipstick assays with set
of different **probes** to target double-stranded DNA
in sample soln.)

IT Membrane filters
(nitrocellulose, in capture zone, oligonucleotide attachment to;
dipstick assays with set of different **probes** to target
double-stranded DNA in sample soln.)

IT Immobilization, **molecular**
(of oligonucleotides at **probe** zone or capture zone of
dipstick; dipstick assays with set of different **probes** to
target double-stranded DNA in sample soln.)

IT Nucleic acid hybridization
(sandwich assay; dipstick assays with set of different **probes**
to target double-stranded DNA in sample soln.)

IT Albumins, biological studies
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(serum, bovine, as capture **probe** spacer in capture zone;
dipstick assays with set of different **probes** to target
double-stranded DNA in sample soln.)

IT 13507-42-1 73423-99-1 247934-65-2
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(as capture **probe** spacer; dipstick assays with set of
different **probes** to target double-stranded DNA in sample
soln.)

IT 2321-07-5D, Fluorescein, oligonucleotide conjugates
RL: ARU (Analytical role, unclassified); ANST (Analytical study)

(as reporter group; dipstick assays with set of different probes to target double-stranded DNA in sample soln.)

- IT 133975-85-6
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (capture probe linked to protein spacer using;
 dipstick assays with set of different probes to
 target double-stranded DNA in sample soln.)
- IT 7440-57-5D, Gold, anti-biotin antibody conjugates
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (colloidal; dipstick assays with set of different probes to
 target double-stranded DNA in sample soln.)
- IT 58-85-5D, Biotin, nucleic-acid coupled
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (dipstick assays with set of different probes to target
 double-stranded DNA in sample soln.)
- IT 9004-70-0, Nitrocellulose
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (filter in capture zone, oligonucleotide attachment to; dipstick assays
 with set of different probes to target double-stranded DNA in
 sample soln.)

L24 ANSWER 3 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:868661 HCAPLUS
 DOCUMENT NUMBER: 136:49292
 TITLE: Detection of RNA targets using INVADER
 oligonucleotide-directed cleavage reactions and
 construction of modified Thermus polymerase enzymes
 with thermostable 5'-nuclease activities
 INVENTOR(S): Allawi, Hatim; Bartholomay, Christian Tor; Chehak,
 Luanne; Curtis, Michelle L.; Eis, Peggy S.; Hall, Jeff
 G.; Ip, Hon S.; Kaiser, Michael; Kwiatkowski, Robert
 W., Jr.; Lukowiak, Andrew A.; Lyamichev, Victor; Ma,
 Wupo; Olson-munoz, Marilyn C.; Olson, Sarah M.;
 Schaefer, James J.; Skrzypczynski, Zbigniew; Takova,
 Tsetska Y.; Vedvik, Kevin L.; Lyamichev, Natalie E.;
 Neri, Bruce P.
 PATENT ASSIGNEE(S): Third Wave Technologies, Inc., USA
 SOURCE: PCT Int. Appl., 1266 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090337	A2	20011129	WO 2001-US17086	20010524
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:			US 2000-577304	A 20000524
			US 2001-758282	A 20010111
			US 2001-864426	A 20010524
			US 2001-864636	A 20010524

AB The present invention provides novel cleavage agents and polymerases for the cleavage and modification of nucleic acid. The cleavage agents and polymerases find use, for example, for the detection and characterization of nucleic acid sequences and variations in nucleic acid sequences. In some embodiments, the 5'-nuclease activity of a variety of modified Thermus polymerase enzymes is used to cleave a target-dependent cleavage structure, thereby indicating the presence of specific nucleic acid sequences or specific variations thereof. The term "cleavage structure" refers to a structure that is formed by the interaction of at least one probe oligonucleotide (called the INVADER oligonucleotide) and a target nucleic acid, forming a structure comprising a duplex, the resulting structure being cleavable by a cleavage agent including but not limited to an enzyme. A sample suspected of contg. the target sequence is contacted with oligonucleotides capable of forming an invasive cleavage structure in the present of the target sequence and with an agent for detecting the presence of the invasive cleavage structure. ARRESTOR oligonucleotides improve sensitivity of multiple sequential invasive cleavage assays and allow use of higher concns. of primary probe without increasing background signal. The detailed description of the invention includes: (1) detection of specific nucleic acid sequences using 5'-nucleases in an INVADER-directed cleavage assay; (2) signal enhancement by incorporating the products of an invasive cleavage reaction into a subsequent invasive cleavage reaction; (3) effect of ARRESTOR oligonucleotides on signal and background in sequential invasive cleavage reactions; (4) improved enzymes for the use in INVADER oligonucleotide-directed cleavage reactions comprising RNA targets; (5) reaction design for INVADER assay detection of RNA targets; (6) kits for performing the RNA invader assay; and (7) the INVADER assay for direct detection and measurement of specific RNA analytes.

IC ICM C12N009-22

ICS C12N009-12; C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 7

L24 ANSWER 4 OF 28 HCAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:781073 HCAPLUS

DOCUMENT NUMBER: 135:328100

TITLE: Detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase

INVENTOR(S): Faruqi, A. Fawad

PATENT ASSIGNEE(S): Molecular Staging, Inc., USA

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001079420	A2	20011025	WO 2001-US11947	20010412
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-547757 A 20000412

AB Disclosed are techniques for detection of nucleic acids, amplification of nucleic acids, or both, involving ligation by T4 RNA ligase of DNA strands hybridized to an RNA strand. These techniques are particularly useful for the detection of RNA sequences and for amplification of nucleic acids from, or dependent on, RNA sequences. It has been discovered that T4 RNA ligase can efficiently ligate DNA ends of nucleic acid strands hybridized to an RNA strand. In particular, this ligation is more efficient than the same ligation carried out with T4 DNA ligase. Thus, techniques involving ligation of DNA ends of nucleic acid strands hybridized to RNA can be performed more efficiently by using T4 RNA ligase. Many known ligation-based detection and amplification techniques are improved through the use of T4 RNA ligase acting on DNA strands or ends. Such techniques include ligase chain reaction (LCR), ligation combined with reverse transcription polymerase chain reaction (RT PCR), ligation-mediated polymerase chain reaction (LMPCR), polymerase chain reaction/ligation detection reaction (PCR/LDR), ligation-dependent polymerase chain reaction (LD-PCR), oligonucleotide ligation assay (OLA), ligation-during-amplification (LDA), ligation of padlock probes, open circle probes, and other circularizable probes, and iterative gap ligation (IGL).

IC ICM C12G

CC 3-1 (Biochemical Genetics)

ST RNA ligase target mediated DNA ligation; amplification RNA DNA probe ligation

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses) (DNA open circle or padlock; detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase)

IT Spheres
(beads, magnetic, coupled to probe; detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase)

IT Fluorescent indicators

Isotope indicators

Phosphorescent substances
(coupled to probe; detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase)

IT Antibodies
Enzymes, biological studies
Ligands
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(coupled to probe; detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase)

IT DNA formation
(rolling-circle, by ligation of two probes; detection and amplification of RNA using target-mediated ligation of DNA by RNA ligase)

L24 ANSWER 5 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:763323 HCPLUS
 DOCUMENT NUMBER: 135:315598
 TITLE: Methods for proteomic analysis using activity based probes for target proteins
 INVENTOR(S): Cravatt, Benjamin F.; Sorensen, Erik; Patricelli, Matthew; Lovato, Martha; Adam, Gregory
 PATENT ASSIGNEE(S): Scripps Research Institute, USA
 SOURCE: PCT Int. Appl., 119 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077684	A2	20011018	WO 2000-US34187	20001215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-195954	P 20000410
			US 2000-212891	P 20000620
			US 2000-222532	P 20000802

OTHER SOURCE(S): MARPAT 135:315598

AB The present invention provides methods for analyzing proteomes, as cells or lysates. The anal. is based on the use of probes that have specificity to the active form of proteins, particularly enzymes and receptors. The probes can be identified in different ways. In accordance with the present invention, a method is provided for generating and screening compd. libraries that are used for the identification of lead mols., and for the parallel identification of their biol. targets. By appending specific functionalities and/or groups to one or more binding moieties, the reactive functionalities gain binding affinity and specificity for particular proteins and classes of proteins. Such libraries of candidate compds., referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biol. activities or target proteins.

IC ICM G01N033-68

ICS G01N033-535; G06F019-00

CC 9-14 (Biochemical Methods)

Section cross-reference(s): 6, 7, 13

ST proteome activity probe synthesis library
 screening protein enzyme receptor

IT Enzyme functional sites

(active; methods for proteomic anal. using activity based probes for target proteins)

IT Labels

(activity-based probes; methods for proteomic anal. using activity based probes for target proteins)

IT Libraries

(chem.; methods for proteomic anal. using activity based probes for target proteins)

IT Functional groups

(cycloalkyl; methods for proteomic anal. using activity based probes for target proteins)

IT Mathematical methods

(dendrograms; methods for proteomic anal. using activity based probes for target proteins)

IT Sulfonates

RL: PRP (Properties)
 (diesters; methods for proteomic anal. using activity

based probes for target proteins)

IT Sulfonic acids, properties
RL: PRP (Properties)
(esters; methods for proteomic anal. using activity based probes for target proteins)

IT Aryl groups
(hetero-; methods for proteomic anal. using activity based probes for target proteins)

IT Functional groups
(heterocycle; methods for proteomic anal. using activity based probes for target proteins)

IT Cell
(lysate fraction; methods for proteomic anal. using activity based probes for target proteins)

IT Enzymes, properties
RL: PRP (Properties)
(metallo-; methods for proteomic anal. using activity based probes for target proteins)

IT Acyl groups
Alkyl groups
Amide group
Aryl groups
Body fluid
Catalysis
Combinatorial library
Drug screening
Electromagnetism
Enzyme kinetics
Genetic methods
Phenotypes
(methods for proteomic anal. using activity based probes for target proteins)

IT Enzymes, analysis
RL: ANT (Analyte); CAT (Catalyst use); PRP (Properties); ANST (Analytical study); USES (Uses)
(methods for proteomic anal. using activity based probes for target proteins)

IT Proteins, general, analysis
Proteome
Receptors
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(methods for proteomic anal. using activity based probes for target proteins)

IT Aldehydes, properties
Amino acids, properties
Epoxides
Isotopes
Ketones, properties
Ligands
Nucleotides, properties
Oligomers
Oligonucleotides
Organic compounds, properties
Polyoxyalkylenes, properties
RL: PRP (Properties)
(methods for proteomic anal. using activity based probes for target proteins)

IT Functional groups

- (phosphoryl group; methods for proteomic anal.
using activity based probes for target
proteins)
- IT Laser ionization mass spectrometry
(photodesorption, matrix-assisted; methods for proteomic
anal. using activity based probes for
target proteins)
- IT Laser desorption mass spectrometry
(photoionization, matrix-assisted; methods for proteomic
anal. using activity based probes for
target proteins)
- IT Denaturation
(protein, thermal; methods for proteomic anal.
using activity based probes for target
proteins)
- IT Functional groups
(pyridyl; methods for proteomic anal. using activity
based probes for target proteins)
- IT Enzymes, analysis
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(redox; methods for proteomic anal. using activity
based probes for target proteins)
- IT Functional groups
(sulfonyl group; methods for proteomic anal. using
activity based probes for target
proteins)
- IT Functional groups
(thiophenyl; methods for proteomic anal. using
activity based probes for target
proteins)
- IT Functional groups
(.alpha.-halocarbonyl; methods for proteomic anal. using
activity based probes for target
proteins)
- IT 38078-09-0, (Diethylamino)sulfur trifluoride
RL: RCT (Reactant)
(DAST; methods for proteomic anal. using activity
based probes for target proteins)
- IT 259270-28-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(FP-biotin; methods for proteomic anal. using
activity based probes for target
proteins)
- IT 259270-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(FP-fluorescein; methods for proteomic anal. using
activity based probes for target
proteins)
- IT 9028-86-8, Aldehyde dehydrogenase
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(cytosolic class I; methods for proteomic anal. using
activity based probes for target
proteins)
- IT 9027-41-2, Hydrolase
RL: ANT (Analyte); CAT (Catalyst use); PRP (Properties); ANST (Analytical
study); USES (Uses)
(methods for proteomic anal. using activity based
probes for target proteins)
- IT 342792-17-0P 342792-18-1P 342792-19-2P 342792-20-5P 342792-21-6P
342792-22-7P 342792-23-8P 342792-24-9P 342792-25-0P 342792-26-1P

342792-27-2P 367480-61-3P
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
 (methods for proteomic anal. using activity based probes for target proteins)

IT 16156-52-8P 117800-97-2P 126092-21-5P
 RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
 (methods for proteomic anal. using activity based probes for target proteins)

IT 52-90-4, Cysteine, properties 56-84-8, L-Aspartic acid, properties 56-86-0, L-Glutamic acid, properties 58-85-5, Biotin 71-00-1, Histidine, properties 107-29-9D, .alpha.-halo derivs. 13537-32-1D, Fluorophosphoric acid, derivs.
 RL: PRP (Properties)
 (methods for proteomic anal. using activity based probes for target proteins)

IT 93-11-8, 2-Naphthalenesulfonyl chloride 98-09-9, Benzenesulfonyl chloride 98-59-9 98-68-0 98-74-8 111-87-5, 1-Octanol, reactions 112-43-6, 10-Undecen-1-ol 112-60-7 121-44-8, Triethylamine, reactions 122-52-1, Triethylphosphite 124-63-0, Methanesulfonyl chloride 2386-60-9, 1-Butanesulfonyl chloride 2857-97-8, Trimethylsilyl bromide 6066-82-6, N-Hydroxysuccinimide 7790-28-5 7795-95-1, 1-Octanesulfonyl chloride 10049-08-8, Ruthenium chloride (RuCl₃) 16629-19-9, 2-Thiophenesulfonyl chloride 18704-37-5, 8-Quinolinesulfonyl chloride 66715-65-9, 2-Pyridylsulfonyl chloride 115416-38-1, 5-(Biotinamido)pentylamine
 RL: RCT (Reactant)
 (methods for proteomic anal. using activity based probes for target proteins)

IT 7766-49-6P 51148-67-5P 52355-50-7P 83637-49-4P 134179-40-1P
 156125-40-5P 259270-26-3P 259270-27-4P 338964-01-5P 338964-02-6P
 338964-03-7P 338964-04-8P 338964-05-9P 338964-06-0P 342792-15-8P
 342792-16-9P 367478-49-7P 367478-57-7P 367478-66-8P 367478-71-5P
 367478-76-0P 367478-80-6P 367478-84-0P 367478-88-4P 367478-96-4P
 367479-00-3P 367479-05-8P 367479-14-9P 367479-19-4P 367479-24-1P
 367479-27-4P 367479-31-0P 367479-35-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (methods for proteomic anal. using activity based probes for target proteins)

IT 367944-46-5 367944-47-6 367944-49-8 367944-51-2 367944-54-5
 368436-43-5 368436-44-6 368436-45-7 368436-46-8 368436-47-9
 RL: PRP (Properties)
 (unclaimed sequence; methods for proteomic anal. using activity based probes for target proteins)

L24 ANSWER 6 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:763309 HCPLUS
 DOCUMENT NUMBER: 135:315597
 TITLE: Methods for bioactivity screening of candidate compounds using activity based probes
 INVENTOR(S): Cravatt, Benjamin F.; Sorensen, Erik; Patricelli, Matthew; Lovato, Martha; Adam, Gregory
 PATENT ASSIGNEE(S): Scripps Research Institute, USA
 SOURCE: PCT Int. Appl., 118 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001077668	A2	20011018	WO 2000-US34167	20001215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-195954	P 20000410
			US 2000-212891	P 20000620
			US 2000-222532	P 20000802

OTHER SOURCE(S): MARPAT 135:315597

AB The present invention provides methods for analyzing proteomes, as cells or lysates. The anal. is based on the use of probes that have specificity to the active form of proteins, particularly enzymes and receptors. The probes can be identified in different ways. In accordance with the present invention, a method is provided for generating and screening compd. libraries that are used for the identification of lead mols., and for the parallel identification of their biol. targets. By appending specific functionalities and/or groups to one or more binding moieties, the reactive functionalities gain binding affinity and specificity for particular proteins and classes of proteins. Such libraries of candidate compds., referred to herein as activity-based probes, or ABPs, are used to screen for one or more desired biol. activities or target proteins.

IC ICM G01N033-10
 ICS G01N033-535; G06F019-00

CC 9-14 (Biochemical Methods)
 Section cross-reference(s): 1, 6, 7, 13, 14

ST proteome activity probe synthesis library
 screening protein enzyme receptor

IT Enzyme functional sites
 (active; methods for bioactivity screening of candidate compds. using activity based probes)

IT Labels
 (activity-based probes; methods for bioactivity screening of candidate compds. using activity based probes)

IT HPLC
 (capillary; methods for bioactivity screening of candidate compds. using activity based probes)

IT Combinatorial library
 (chem.; methods for bioactivity screening of candidate compds. using activity based probes)

IT Sulfonic acids, properties
 RL: PRP (Properties)
 (esters; methods for bioactivity screening of candidate compds. using activity based probes)

IT Functional groups
 (fluorophosphonyl; methods for bioactivity screening of candidate compds. using activity based probes)

IT Ketones, properties
 RL: PRP (Properties)
 (halo; methods for bioactivity screening of candidate compds. using

activity based probes)

IT Enzymes, properties
RL: PRP (Properties)
(metallo-; methods for bioactivity screening of candidate compds. using activity based probes)

IT Capillary electrophoresis
Cell
Computer application
Computer program
Drug screening
Drugs
Electromagnetism
Immobilization, biochemical
Infection
Mass spectrometry
Phenotypes
Radiochemical analysis
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Receptors
RL: ANT (Analyte); BPR (Biological process); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Enzymes, analysis
RL: ANT (Analyte); CAT (Catalyst use); PRP (Properties); ANST (Analytical study); USES (Uses)
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Proteins, general, analysis
Proteome
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Ligands
RL: BPR (Biological process); PRP (Properties); BIOL (Biological study); PROC (Process)
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Epoxides
RL: PRP (Properties)
(methods for bioactivity screening of candidate compds. using activity based probes)

IT Functional groups
(phosphoryl group, fluoro-; methods for bioactivity screening of candidate compds. using activity based probes)

IT Functional groups
(sulfonyl group; methods for bioactivity screening of candidate compds. using activity based probes)

IT 38078-09-0, (Diethylamino)sulfur trifluoride
RL: RCT (Reactant)
(DAST; methods for bioactivity screening of candidate compds. using activity based probes)

IT 259270-28-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(FP-biotin; methods for bioactivity screening of candidate compds. using activity based probes)

IT 259270-29-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(FP-fluorescein; methods for bioactivity screening of candidate compds.)

using activity based probes)

IT 9028-86-8, Aldehyde dehydrogenase
 RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
 (cytosolic class I; methods for bioactivity screening of candidate compds. using activity based probes)

IT 9027-41-2, Hydrolase
 RL: ANT (Analyte); CAT (Catalyst use); PRP (Properties); ANST (Analytical study); USES (Uses)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 342792-17-0P 342792-18-1P 342792-19-2P 342792-20-5P 342792-21-6P
 342792-22-7P 342792-23-8P 342792-24-9P 342792-25-0P 342792-26-1P
 342792-27-2P 367480-61-3P
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 16156-52-8P 117800-97-2P 126092-21-5P
 RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 52-90-4, L-Cysteine, properties 56-45-1, L-Serine, properties 56-84-8,
 L-Aspartic acid, properties 56-86-0, L-Glutamic acid, properties
 71-00-1, L-Histidine, properties 107-29-9D, .alpha.-halo derivs.
 7723-14-0D, Phosphorus, fluoro derivs. 7782-41-4, Fluorine, properties
 13537-32-1D, Fluorophosphoric acid, derivs.
 RL: PRP (Properties)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 58-85-5, Biotin
 RL: PRP (Properties); RCT (Reactant)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 93-11-8, 2-Naphthalenesulfonyl chloride 98-09-9, Benzenesulfonyl chloride 98-59-9 98-68-0 98-74-8 111-87-5, 1-Octanol, reactions 112-43-6, 10-Undecen-1-ol 112-60-7 121-44-8, Triethylamine, reactions 122-52-1, Triethylphosphite 124-63-0, Methanesulfonyl chloride 2386-60-9, 1-Butanesulfonyl chloride 2857-97-8, Trimethylsilyl bromide 6066-82-6, N-Hydroxysuccinimide 7681-82-5, Sodium iodide (NaI), reactions 7795-95-1, 1-Octanesulfonyl chloride 10049-08-8, Ruthenium chloride (RuCl₃) 16629-19-9, 2-Thiophenesulfonyl chloride 18704-37-5, 8-Quinolinesulfonyl chloride 66715-65-9, 2-Pyridylsulfonyl chloride 115416-38-1, 5-(Biotinamido)pentylamine
 RL: RCT (Reactant)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 7766-49-6P 51148-67-5P 52355-50-7P 83637-49-4P 134179-40-1P
 156125-40-5P 259270-26-3P 259270-27-4P 338964-01-5P 338964-02-6P
 338964-03-7P 338964-04-8P 338964-05-9P 338964-06-0P 342792-15-8P
 342792-16-9P 367478-49-7P 367478-57-7P 367478-66-8P 367478-71-5P
 367478-76-0P 367478-80-6P 367478-84-0P 367478-88-4P 367478-96-4P
 367479-00-3P 367479-05-8P 367479-14-9P 367479-19-4P 367479-24-1P
 367479-27-4P 367479-31-0P 367479-35-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (methods for bioactivity screening of candidate compds. using activity based probes)

IT 367944-46-5 367944-47-6 367944-48-7 367944-49-8 367944-50-1
 367944-51-2 367944-53-4 367944-54-5 367944-55-6 367944-57-8
 RL: PRP (Properties)

(unclaimed sequence; methods for bioactivity screening of candidate compds. using **activity based probes**)

L24 ANSWER 7 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:757545 HCPLUS
 DOCUMENT NUMBER: 136:66000
 TITLE: Direct visualization of serine hydrolase activities in complex proteomes
 using fluorescent active site-directed probes
 AUTHOR(S): Patricelli, Matthew P.; Giang, Dan K.; Stamp, Lisa M.;
 Burbam, Jonathan J.
 CORPORATE SOURCE: ActivX Biosciences, La Jolla, CA, 92037, USA
 SOURCE: Proteomics (2001), 1(9), 1067-1071
 Published in: Electrophoresis, 22(16)
 CODEN: PROTC7; ISSN: 1615-9853
 PUBLISHER: Wiley-VCH Verlag GmbH
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The field of biochem. is currently faced with the enormous challenge of assigning functional significance to more than thirty thousand predicted protein products encoded by the human genome. In order to accomplish this daunting task, methods will be required that facilitate the global anal. of proteins in complex biol. systems. Recently, methods have been described for simultaneously monitoring the activity of multiple enzymes in crude proteomes based on their reactivity with tagged chem. probes. These activity based probes (ABPs) have used either radiochem. or biotin/avidin-based detection methods to allow consolidated visualization of numerous enzyme activities. Here we report the synthesis and evaluation of fluorescent activity based probes for the serine hydrolase super-family of enzymes. The fluorescent methods detailed herein provide superior throughput, sensitivity, and quant. accuracy when compared to previously described ABPs, and provide a straight-forward platform for high-throughput proteome anal.

CC 7-1 (Enzymes)
 ST serine hydrolase detection proteome fluorescent probe; active site probe serine hydrolase proteome
 IT Fluorometry
 (direct visualization of serine hydrolase **activities** in complex **proteomes** using fluorescent active site-directed probes)
 IT **Proteome**
 RL: AMX (Analytical matrix); ANST (Analytical study)
 (direct visualization of serine hydrolase **activities** in complex **proteomes** using fluorescent active site-directed probes)
 IT 9015-88-7, D-Serine dehydrase 153301-19-0, Fatty acid amide hydrolase
 RL: ANT (Analyte); ANST (Analytical study)
 (direct visualization of serine hydrolase **activities** in complex **proteomes** using fluorescent active site-directed probes)
 IT 383912-85-4P 383912-86-5P
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
 (direct visualization of serine hydrolase **activities** in complex **proteomes** using fluorescent active site-directed probes)
 IT 87328-05-0 338964-06-0 383912-87-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (direct visualization of serine hydrolase **activities** in complex **proteomes** using fluorescent active site-directed

probes)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 8 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:748054 HCPLUS
 DOCUMENT NUMBER: 135:299485
 TITLE: Compositions and methods for detecting and quantifying gene expression in microarrays
 INVENTOR(S): Lowe, David G.; Marsters, James C. Jr; Robbie, Edward P.; Smith, Victoria
 PATENT ASSIGNEE(S): Genentech, Inc., USA
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001075166	A2	20011011	WO 2001-US10482	20010330
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 2000-193767 P 20000331

AB Compns. and methods for improving detection sensitivity in nucleic acid microarray anal. are disclosed, including methods of purifying nucleic acids, methods of synthesizing fluorescent DNA probes, methods of hybridization, and methods of activating a substrate for target mol. attachment. The compns. and methods of this invention include synthesis of cDNA, sDNA, or rRNA probes from cellular RNA by in vitro transcription and/or a single-round of reverse transcription with incorporation of fluorochromes. Specific procedures for microarray slide prepn. to decrease background fluorescence are given. For example, silanization of glass slides with toluene as the solvent is preferred. In addn., unmodified polynucleotides can attach to a glass slide treated with 3-aminopropyltriethoxysilane followed by phenylene diisothiocyanate. Modified target DNA can also be synthesized using PCR primers which contain a primary amine and an alkyl linker attached to the 5'-end. The modified target DNA is then reacted with activated silanized glass slides. Microarray hybridization buffers contg. alkylammonium salts, dimethylsulfoxide and formamide and lacking the detergent sodium dodecyl sulfate also improved the detection sensitivity. The invention is illustrated with microarrays hybridized with fluorescent probes synthesized from very small quantities of RNA isolated from microdissected tumor cells, paraffin-embedded liver and colon tissue, fresh frozen liver tissue, and fresh frozen colon tissue. The microarray expts. were designed to compare tissue sample prepn. methods and gene expression in tumor vs. healthy tissues. An example of the sensitivity of these methods shows a microarray hybridized with sDNA probes from one round of amplification of 2 pg of RNA from an ovarian carcinoma cell line.

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 9, 14, 21

ST DNA microarray technol sensitivity fluorescent **probe**
hybridization target attachment; microarray substrate linker cRNA cDNA
expression **probe** amplification diagnosis

IT Animal tissue
Body fluid
Cell
Ceramic composites
DNA microarray technology
Fluorescent probes
Gene dosage
Laser fluorometry
Nucleic acid hybridization
Printing (impact)
Printing (nonimpact)
UV and visible spectroscopy
(compns. and methods for detecting and quantifying gene expression in
microarrays)

IT **Functional groups**
(hydroxysilyl, attached **target mol.** or linker;
compns. and methods for detecting and quantifying gene expression in
microarrays)

IT Antibodies
DNA
Ligands
Oligonucleotides
Peptide nucleic acids
Proteins, general, biological studies
RNA
Receptors
cDNA
mRNA
RL: ANT (Analyte); BUU (Biological use, unclassified); DEV (Device
component use); ANST (Analytical study); BIOL (Biological study); USES
(Uses)
(immobilized; compns. and methods for detecting and quantifying gene
expression in microarrays)

IT **Probes** (nucleic acid)
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BUU
(Biological use, unclassified); ANST (Analytical study); BIOL (Biological
study); PREP (Preparation); USES (Uses)
(labeled; compns. and methods for detecting and quantifying gene
expression in microarrays)

IT Analytical apparatus
Microanalysis
(microarray, RNA, peptide nucleic acid, polypeptide, **protein**,
antibody, receptor, or **ligand**; compns. and methods for
detecting and quantifying gene expression in microarrays)

IT Nucleic acid amplification (method)
(sDNA and cRNA **probe** synthesis; compns. and methods for
detecting and quantifying gene expression in microarrays)

IT 302-04-5, Thiocyanate, biological studies
RL: BUU (Biological use, unclassified); DEV (Device component use); RCT
(Reactant); BIOL (Biological study); USES (Uses)
(**functional group**, linker reagent; compns. and
methods for detecting and quantifying gene expression in microarrays)

IT 247144-99-6D, Alexa 488, conjugated with dUTP 247145-23-9D, Alexa 546,
conjugated with dUTP
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)

(labeled probe; compns. and methods for detecting and quantifying gene expression in microarrays)

L24 ANSWER 9 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:709832 HCAPLUS
 DOCUMENT NUMBER: 135:238953
 TITLE: Method for identifying cell-specific target structures by immunolabeling
 INVENTOR(S): Schubert, Walter
 PATENT ASSIGNEE(S): Germany
 SOURCE: Eur. Pat. Appl., 6 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1136822	A2	20010926	EP 2001-106571	20010315
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
DE 10014685	A1	20011031	DE 2000-10014685	20000324
US 2001039023	A1	20011108	US 2001-808224	20010314
JP 2001309799	A2	20011106	JP 2001-86054	20010323
CN 1334463	A	20020206	CN 2001-109720	20010323

PRIORITY APPLN. INFO.: DE 2000-10014685 A 20000324

AB In a procedure for identification of cell-specific target structures, reagent soln. Y1 (contg. at least one marker mol., e.g. a fluorescently labeled antibody) is automatically applied to object X1 (including cells and/or cell membranes from a cell or tissue sample). After reaction, automatic detection is used to recognize X1 labeled by Y1. Reagent Y1 is removed before or after detection of labeled material, and further reagent solns. Yn (n = 2, 3...n) may be applied for labeling; likewise, further objects of similar nature Xn (n = 2, 3...n) may be processed through these steps. At least one difference is detd. between the labeled forms of object X1 and object Xn. Identification is made of reagent soln. Y1 or Yn causing the difference in the previous step. Mols. of mol. complexes are then selected and characterized (esp. by protein sepn. techniques) in relation to binding to the reagents.

IC ICM G01N033-68
 ICS G01N001-30

CC 9-10 (Biochemical Methods)

ST cell target protein identification immunolabeling

IT Animal tissue

Cell

Cell membrane

Fluorescent probes

Imaging

(method for identifying cell-specific target structures by immunolabeling)

IT Proteins, general, analysis

RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(method for identifying cell-specific target structures by immunolabeling)

IT Ligands

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)

(method for identifying cell-specific target structures by immunolabeling)

L24 ANSWER 10 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:661595 HCAPLUS
 DOCUMENT NUMBER: 135:224727
 TITLE: The g12L gene and protein associated with the control of metabolic activity and thermogenesis in brown adipose tissue
 INVENTOR(S): Lewin, David A.; Adams, Sean H.
 PATENT ASSIGNEE(S): Curagen Corp., USA; Genentech, Inc.
 SOURCE: PCT Int. Appl., 105 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001064884	A2	20010907	WO 2001-US6839	20010302
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 2000-186513	P 20000302

AB Disclosed herein are novel human and mouse nucleic acid sequences that encode polypeptides. Also disclosed are polypeptides encoded by these nucleic acid sequences, and antibodies that immunospecifically-bind to the polypeptide, as well as derivs., variants, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or antibody. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel nucleic acids and proteins. The protein was identified as similar to the rat Spot14 protein. The levels of the protein in mouse brown adipose tissue parallel those seen for Spot14 in rat brown adipose tissue. These criteria were used to screen for genes showing regulated expression in brown adipose tissue.

IC ICM C12N015-12
 ICS C07K014-47; C12N005-10; C07K016-18; G01N033-53; C12Q001-68;
 A61K038-17

CC 13-6 (Mammalian Biochemistry)
 Section cross-reference(s): 3

ST g12L protein cDNA human mouse cloning sequence; brown adipose tissue thermoregulation g12L protein gene discovery

IT Adipose tissue
 (brown; g12L gene and protein assocd. with control of metabolic activity and thermogenesis in brown adipose tissue)

IT Metabolism, animal
 (disorder, g12L protein as target in treatment of; g12L gene and protein assocd. with control of metabolic activity and thermogenesis in brown adipose tissue)

IT Nucleic acid hybridization
 (for detection of g12L gene expression; g12L gene and protein assocd. with control of metabolic activity and thermogenesis in brown adipose tissue)

IT Probes (nucleic acid)

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(for detection of g12L gene expression; g12L gene and **protein**
assocd. with control of metabolic **activity** and thermogenesis
in brown adipose tissue)

IT Drug screening
(for effectors of g12L **protein**; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)

IT Immunoassay
(for g12L **protein**; g12L gene and **protein** assocd.
with control of metabolic activity and thermogenesis in brown adipose
tissue)

IT Neoplasm
(g12L **protein** as marker for; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)

IT Cachexia
Diabetes mellitus
Obesity
(g12L **protein** as **target** in treatment of; g12L gene
and **protein** assocd. with control of metabolic activity and
thermogenesis in brown adipose tissue)

IT Gene, animal
RL: BSU (Biological study, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(g12L; g12L gene and **protein** assocd. with control of
metabolic activity and thermogenesis in brown adipose tissue)

IT Genetic methods
(gene discovery, of g12L gene of human and mouse; g12L gene and
protein assocd. with control of metabolic activity and
thermogenesis in brown adipose tissue)

IT Mouse
(gene g12L of human and; g12L gene and **protein** assocd. with
control of metabolic activity and thermogenesis in brown adipose
tissue)

IT Proteins, specific or class
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);
BIOL (Biological study); PROC (Process); USES (Uses)
(gene g12L; g12L gene and **protein** assocd. with control of
metabolic activity and thermogenesis in brown adipose tissue)

IT Chromosome
(human X, g12L gene mapping to; g12L gene and **protein** assocd.
with control of metabolic activity and thermogenesis in brown adipose
tissue)

IT Antibodies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(humanized, to g12L **protein**; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)

IT Antibodies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal, to g12L **protein**; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)

IT Chromosome
(mouse X, DXMit86, g12L gene mapping to; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)

- IT Genetic mapping
cDNA sequences
(of g12L gene of human and mouse; g12L gene and **protein**
assocd. with control of metabolic activity and thermogenesis in brown
adipose tissue)
- IT **Protein** motifs
(of g12L gene product; g12L gene and **protein** assocd. with
control of metabolic activity and thermogenesis in brown adipose
tissue)
- IT **Protein** sequences
(of g12L gene products of human and mouse; g12L gene and
protein assocd. with control of metabolic activity and
thermogenesis in brown adipose tissue)
- IT Antibodies
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(to g12L **protein**; g12L gene and **protein** assocd.
with control of metabolic activity and thermogenesis in brown adipose
tissue)
- IT 326056-57-9, **Protein** g12L (mouse gene g12L) 358797-39-4,
Protein g12L (human gene g12L)
RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);
BIOL (Biological study); PROC (Process); USES (Uses)
(amino acid sequence; g12L gene and **protein** assocd. with
control of metabolic activity and thermogenesis in brown adipose
tissue)
- IT 358797-38-3 358797-40-7
RL: BSU (Biological study, unclassified); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; g12L gene and **protein** assocd. with
control of metabolic activity and thermogenesis in brown adipose
tissue)
- IT 170085-96-8 186513-34-8 186513-35-9
RL: PRP (Properties)
(unclaimed **protein** sequence; g12L gene and **protein**
assocd. with the control of metabolic activity and thermogenesis in
brown adipose tissue)

L24 ANSWER 11 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:630982 HCPLUS
 DOCUMENT NUMBER: 135:191238
 TITLE: Diagnosis method using gene chip containing primers
for genes of leukocyte differentiation antigens
 INVENTOR(S): Yang, Mengsu; Miao, Jinming
 PATENT ASSIGNEE(S): Hong Kong
 SOURCE: Faming Zhanli Shenqing Gongkai Shuomingshu, 22 pp.
 CODEN: CNXXEV
 DOCUMENT TYPE: Patent
 LANGUAGE: Chinese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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CN 1284568	A	20010221	CN 1999-110796	19990813

AB The nucleotide sequences of probes targeted to 172 CD antigen genes for
diagnosis are presented. The probes consist of fluorescent labeling
substance at 5' end (not specified), C6 alkyl linker, and nucleotide
sequence targeted to CD antigen genes. The gene chip is manufd. by
synthesizing 20-60 bp DNA probes, spotting on Si sheet or glass sheet.

The detection process comprises isolating mRNA from samples, purifn., reverse-transcription to obtain cDNA, labeling, hybridizing with DNA chip, and detecting fluorescent intensity. The method is useful for diagnosing blood diseases and matching donor/acceptor in organ transplantation.

IC ICM C12Q001-68

ICS G01N033-50

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 15

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(4F2 antigen, gene chip probes for the gene of; diagnosis
method using gene chip contg. primers for genes of leukocyte
differentiation antigens)

IT Complement receptors

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(C5a, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD100, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD101, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD103, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD104, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD105, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD107a, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD107b, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD114, gene chip probes for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(CD114a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD114b, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD115, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD116, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD117, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD121a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD123, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD124, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD126, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD127, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD130, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD132, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

- (CD134, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD135, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD138, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD140a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD140b, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD141, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD142, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD143, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD144, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD147, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD148, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD151, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(CD153, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD155, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD157, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD161, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD162, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD163, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD164, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD166, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT CD1 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD1a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT CD1 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD1b, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT CD1 (antigen)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD1c, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD1d, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(CD1e, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD24, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD27, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD29a, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD29b, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD32b2, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD32b3, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD33, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD37, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD39, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD3d, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD3e, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

- (CD3g, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Glycoproteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD40-L (antigen CD40 ligand), gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD41, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD42a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD42b, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD42c, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD42d, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD44R, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD47, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD48, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD49a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD49f, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(CD52, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD53, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD6, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD63, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66a, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66b, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66c, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66d, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66e, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD66f, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD70, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT CD antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD72, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(CD73, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD79a, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD79b, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD83, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD87, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD89, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD8a, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD8b1, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD8b2, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD8b3, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT CD antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD9, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD90, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Antigens

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

- (CD91, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD94, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD96, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD97, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CD99, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw119, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw121b, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw125, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw128a, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw128b, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw131, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw136, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

- (CDw137, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(CDw150, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Selectins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(E-, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Cell adhesion molecules
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ICAM-1 (intercellular adhesion mol. 1), gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Cell adhesion molecules
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ICAM-2 (intercellular adhesion mol. 2), gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Cell adhesion molecules
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(ICAM-3 (intercellular adhesion mol. 3), gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Immunoglobulin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IgE type II, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Immunoglobulin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IgG type I, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Immunoglobulin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(IgG type IIA, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Selectins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(L-, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Glycoproteins, specific or class
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(MCP (membrane cofactor **protein**), gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Antigens
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(MUC18, gene chip **probes** for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)
- IT Selectins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(P-, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Cell adhesion molecules

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(PECAM-1, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Proteins, specific or class

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(TAPA-1 (target of antiproliferative antibody, 1), gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Cell adhesion molecules

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(VCAM-1, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antigens CD11a, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antigens CD11b, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(antigens CD11c, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Glycoproteins, specific or class

RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(gene KAI1, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Antigens

Antigens

CD14 (antigen)

CD19 (antigen)

CD2 (antigen)

CD20 (antigen)

CD22 (antigen)

CD26 (antigen)

CD28 (antigen)

CD30 (antigen)

CD34 (antigen)

CD36 (antigen)

CD38 (antigen)

CD4 (antigen)

CD40 (antigen)

CD44 (antigen)

CD45 (antigen)

CD5 (antigen)

CD56 (antigen)

CD59 (antigen)

CD68 (antigen)

CD69 (antigen)

CD7 (antigen)
CD80 (antigen)
CD86 (antigen)
CTLA-4 (antigen)
Fas antigen
Invariant chain (class II antigen)
LFA-3 (antigen)
Leukosialin
Transferrin receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(gene chip **probes** for the gene of; diagnosis method using
gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Primers (nucleic acid)
Probes (nucleic acid)
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical
study); USES (Uses)
(of CD antigen gene; diagnosis method using gene chip contg. primers
for genes of leukocyte differentiation antigens)

IT Tumor necrosis factor receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p60, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Tumor necrosis factor receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(p80, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Glass, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(**probe** immobilized to; diagnosis method using gene chip
contg. primers for genes of leukocyte differentiation antigens)

IT Complement receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(type 1, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Complement receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(type 2, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT TCR (T cell receptors)
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.zeta., gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Interleukin 2 receptors
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha.-chain, gene chip **probes** for the gene of; diagnosis
method using gene chip contg. primers for genes of leukocyte
differentiation antigens)

IT Integrins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(.alpha.v, gene chip **probes** for the gene of; diagnosis method
using gene chip contg. primers for genes of leukocyte differentiation
antigens)

IT Integrins
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)

(.alpha.2, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.alpha.3, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.alpha.4, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.alpha.5, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Interleukin 2 receptors
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.beta.-chain, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.beta.2, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT Integrins
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
 (.beta.3, gene chip probes for the gene of; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

IT 7440-21-3, Silicon, analysis
 RL: ARU (Analytical role, unclassified); ANST (Analytical study)
 (probe immobilized to; diagnosis method using gene chip contg. primers for genes of leukocyte differentiation antigens)

L24 ANSWER 12 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:397084 HCPLUS
 DOCUMENT NUMBER: 135:15064
 TITLE: Oligonucleotides and assemblies thereof and method for detection of target nucleic acid sequences
 INVENTOR(S): Alajem, Sara; Reinhartz, Avraham; Waksman, Michal
 PATENT ASSIGNEE(S): Gamida Sense Diagnostics Ltd., Israel
 SOURCE: PCT Int. Appl., 97 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001038570	A1	20010531	WO 2000-IL798	20001129
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,			

YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-449545 A 19991129

- AB An oligonucleotide or assembly of oligonucleotides for the detection of the presence or absence of a target nucleic acid in a sample. The assembly of oligonucleotides comprises four regions, a first and second regions which hybridize to the target nucleic acid sequence and a third and fourth region where the third region is linked to the first region and the second region is linked to the fourth region. The third and fourth regions hybridize to one another. This hybridized structure can be cleaved with a restriction enzyme, which cleavage will indicate hybridization of the oligonucleotide or oligonucleotides to the target. The invention also comprises methods of using these oligonucleotides.
- IC ICM C12Q001-68
 ICS C12Q001-70; C12P019-34; C07H021-02; C07H021-04
- CC 3-1 (Biochemical Genetics)
- IT Avidins
 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (conjugates with oligonucleotide probes; oligonucleotides and assemblies thereof and method for detection of target nucleic acid sequences)
- IT Oligonucleotides
Probes (nucleic acid)
 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (double-strand-, restriction site-forming, fluorophore-labeled; oligonucleotides and assemblies thereof and method for detection of target nucleic acid sequences)
- IT Chelating agents
 Epitopes
 Fluorescent substances
 Ions
 (oligonucleotide probes labeled with; oligonucleotides and assemblies thereof and method for detection of target nucleic acid sequences)
- IT Antibodies
 Antigens
Enzymes, biological studies
Ligands
 Radionuclides, biological studies
 Receptors
 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (oligonucleotide probes labeled with; oligonucleotides and assemblies thereof and method for detection of target nucleic acid sequences)
- IT 58-85-5D, Biotin, conjugates with oligonucleotide probes
 6268-49-1D, conjugates with oligonucleotide probes 9013-20-1D,
 Streptavidin, conjugates with oligonucleotide probes
 50402-56-7D, EDANS, conjugates with oligonucleotide probes
 RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
 (oligonucleotides and assemblies thereof and method for detection of

target nucleic acid sequences)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 13 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:247291 HCAPLUS
 DOCUMENT NUMBER: 134:261221
 TITLE: Methods for creating a compound library and identifying lead chemical templates and ligands for target molecules
 INVENTOR(S): Stockman, Brian J.; Farley, Kathleen
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001023330	A2	20010405	WO 2000-US41034	20000929
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1999-156818	P 19990929
			US 1999-161682	P 19991026
			US 2000-192685	P 20000328

AB A method for developing a library of compds., the compd. library, a method for identifying ligands for target mols., and a method for identifying lead chem. templates, which, for example, can be used in drug discovery and design, are provided. Certain embodiments of these methods include the use of NMR spectroscopy.
 IC ICM C07B061-00
 ICS G01N033-53; G01R033-46
 CC 1-1 (Pharmacology)
 ST drug design library ligand identification NMR
 IT Desulfovibrio vulgaris
 (flavodoxin; methods for creating compd. library and identifying lead chem. templates and ligands for target mols
 .)
 IT Antibacterial agents
 Antiviral agents
 Combinatorial library
 Drug design
 Drug screening
 Flow injection systems
 Microtiter plates
 Molecular association
 NMR spectroscopy
 Proton NMR spectroscopy
 (methods for creating compd. library and identifying lead chem.
 templates and ligands for target mols.)
 IT Flavodoxin

Ligands
Proteins, general, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(methods for creating compd. library and identifying lead chem.
templates and ligands for target mols.)
IT Holders
(multiwell sample holder; methods for creating compd. library and
identifying lead chem. templates and ligands for
target mols.)
IT NMR spectroscopy
(nitrogen-15; methods for creating compd. library and identifying lead
chem. templates and ligands for target mols
.)
IT NMR spectroscopy
(two-dimensional; methods for creating compd. library and identifying
lead chem. templates and ligands for target
mols.)
IT Overhauser effect
(water-ligand; methods for creating compd. library and
identifying lead chem. templates and ligands for
target mols.)
IT NMR spectrometers
(with flow-injection probe; methods for creating compd.
library and identifying lead chem. templates and ligands for
target mols.)
IT 7789-20-0, Water-d2
RL: MSC (Miscellaneous)
(methods for creating compd. library and identifying lead chem.
templates and ligands for target mols.)
IT 120-72-9D, Indole, derivs.
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(methods for creating compd. library and identifying lead chem.
templates and ligands for target mols.)
IT 90-52-8 21404-88-6 144477-54-3
RL: PRP (Properties)
(methods for creating compd. library and identifying lead chem.
templates and ligands for target mols.)
IT 7732-18-5, Water, processes
RL: PEP (Physical, engineering or chemical process); PROC (Process)
(water-ligand NOE; methods for creating compd. library and
identifying lead chem. templates and ligands for
target mols.)

L24 ANSWER 14 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:175793 HCPLUS
DOCUMENT NUMBER: 135:16295
TITLE: Profiling the specific reactivity of the
proteome with non-directed activity
-based probes
AUTHOR(S): Adam, Gregory C.; Cravatt, Benjamin F.; Sorensen, Erik
J.
CORPORATE SOURCE: The Skaggs Institute for Chemical Biology and
Department of Chemistry, The Scripps Research
Institute, La Jolla, CA, 92037, USA
SOURCE: Chemistry & Biology (2001), 8(1), 81-95
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background: The field of proteomics aims to characterize dynamics in

protein function on a global level. However, several classes of proteins, in particular low abundance proteins, remain difficult to characterize using std. proteomics technologies. Recently, chem. strategies have emerged that profile classes of proteins based on activity rather than quantity, thereby greatly facilitating the anal. of low abundance constituents of the proteome. Results: In order to expand the classes of proteins susceptible to anal. by activity-based methods, we have synthesized a library of biotinylated sulfonate esters and applied its members to complex proteomes under conditions that distinguish patterns of specific protein reactivity. Individual sulfonates exhibited unique profiles of proteome reactivity that in extreme cases appeared nearly orthogonal to one another. A robustly labeled protein was identified as a class I aldehyde dehydrogenase and shown to be irreversibly inhibited by members of the sulfonate library. Conclusions: Through screening the proteome with a nondirected library of chem. probes, diverse patterns of protein reactivity were uncovered. These probes labeled protein targets based on properties other than abundance, circumventing one of the major challenges facing contemporary proteomics research. Considering further that the probes were found to inhibit a target enzyme's catalytic activity, the methods described herein should facilitate the identification of compds. possessing both selective proteome reactivities and novel bioactivities.

- CC 9-16 (Biochemical Methods)
 Section cross-reference(s): 6, 7, 13
 ST **protein activity based probe** biotinylated sulfonate ester aldehyde dehydrogenase; **proteome activity based probe** biotinylated sulfonate ester aldehyde dehydrogenase
 IT Labels
 (activity-based probes; profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
 IT Protein sequences
 (aldehyde dehydrogenase; profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
 IT Proteins, specific or class
 RL: ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
 (labeled; profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
 IT Enzyme kinetics
 Testis
 (profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
 IT Enzymes, analysis
 Proteins, general, analysis
 Proteome
 RL: ANT (Analyte); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PROC (Process)
 (profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
 IT 9028-86-8P, Aldehyde dehydrogenase
 RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); PROC (Process)

(class I; profiling specific reactivity of **proteome** with non-directed **activity-based probes**)

- IT 16156-52-8P 117800-97-2P 126092-21-5P 342792-17-0P 342792-18-1P
 342792-19-2P 342792-20-5P 342792-21-6P 342792-22-7P 342792-23-8P
 342792-24-9P 342792-25-0P 342792-26-1P 342792-27-2P
 RL: ARG (Analytical reagent use); ARU (Analytical role, unclassified); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
 (profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
- IT 64-17-5, Ethanol, reactions 111-87-5, 1-Octanol, reactions 112-43-6,
 10-Undecen-1-ol 124-63-0, Methanesulfonyl chloride 66715-65-9,
 2-Pyridylsulfonyl chloride 115416-38-1
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (profiling specific reactivity of **proteome** with non-directed **activity-based probes**)
- IT 342792-15-8P 342792-16-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (profiling specific reactivity of **proteome** with non-directed **activity-based probes**)

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 15 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:101352 HCPLUS
 DOCUMENT NUMBER: 134:158458
 TITLE: **Probes** for detecting nucleic acid target sequences involving in vitro transcription from an RNA polymerase promoter
 INVENTOR(S): Lloyd, John Scott; Weston, Anthony; Cardy, Donald Leonard Nicholas; Marsh, Peter
 PATENT ASSIGNEE(S): Cytocell Limited, UK
 SOURCE: PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009376	A1	20010208	WO 2000-GB2946	20000731
W: AU, CA, JP, US RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: GB 1999-17816 A 19990729
 AB Disclosed is a probe mol. comprising single stranded nucleic acid; said probe comprising a single stranded sequence complementary to a target nucleic acid sequence; a single strand of an RNA polymerase promoter sequence; and a blocking moiety adjacent or substantially adjacent to the promoter sequence, a method of detecting a nucleic acid sequence of interest using the probe; and kits comprising the probe.
 IC ICM C12Q001-68
 CC 3-1 (Biochemical Genetics)
 ST nucleic acid **probe** oligonucleotide RNA polymerase promoter transcription
 IT Functional groups

(C2-C20 or C3-C10 alkyl, alkanol or alkylene, blocking moiety comprising; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT Enzymes, biological studies

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(as marker; method for detecting nucleic acid **target** sequences involving in vitro transcription from RNA polymerase promoter)

IT Test kits

(comprising **probes** of this invention; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT Oligonucleotides

RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)

(labeled, as **probe** to RNA polymerase promoter; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT Nucleic acids

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(locked, LNA, **probe** comprising; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT Peptide nucleic acids

RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)

(**probe** comprising; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT DNA

RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)

(single-stranded, **probe** comprising; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT Probes (nucleic acid)

RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical study); USES (Uses)

(to RNA polymerase promoter; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT 325177-26-2

RL: PRP (Properties)

(Unclaimed; **probes** for detecting nucleic acid target sequences involving in vitro transcription from an RNA polymerase promoter)

IT 9012-90-2, DNA polymerase

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(for extending **probe** 3'-end; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT 2615-15-8, Hexaethylene glycol 26264-14-2, Propanediol 26762-67-4, Octanediol

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(**probe** comprising; method for detecting nucleic acid target sequences involving in vitro transcription from RNA polymerase promoter)

IT 324589-37-9 324589-38-0 324589-41-5 324589-42-6 325177-18-2, 1:
 PN: WO0109376 SEQID: 1 unclaimed DNA 325177-19-3, 2: PN: WO0109376
 SEQID: 2 unclaimed DNA 325177-20-6, 3: PN: WO0109376 SEQID: 3 unclaimed
 DNA 325177-21-7, 4: PN: WO0109376 SEQID: 4 unclaimed DNA 325177-22-8,
 5: PN: WO0109376 SEQID: 5 unclaimed DNA 325177-23-9, 8: PN: WO0109376
 SEQID: 8 unclaimed DNA 325177-24-0, 9: PN: WO0109376 SEQID: 9 unclaimed
 DNA 325177-25-1 325177-27-3 325177-28-4 325177-29-5 325177-30-8
 325177-31-9 325177-32-0 325177-33-1 325177-34-2 325177-35-3
 325177-36-4 325177-37-5 325177-38-6 325177-39-7

RL: PRP (Properties)

(unclaimed nucleotide sequence; probes for detecting nucleic acid target sequences involving in vitro transcription from an RNA polymerase promoter)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 16 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:814669 HCPLUS
 DOCUMENT NUMBER: 133:346790
 TITLE: Multiple tag analysis
 INVENTOR(S): Lizardi, Paul M.; Latimer, Darin R.
 PATENT ASSIGNEE(S): Yale University, USA
 SOURCE: PCT Int. Appl., 96 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000068434	A2	20001116	WO 2000-US12391	20000505
WO 2000068434	A3	20020131		
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 1999-132969 P 19990507

AB Disclosed is a method of detecting multiple analytes in a sample in a single assay. The method is based on encoding target mols. with signals followed by decoding of the encoded signal. This encoding/decoding uncouples the detection of a target mol. from the chem. and phys. properties of the target mol. In basic form, the disclosed method involves assocn. of one or more reporter mols. with one or more target samples, assocn. of one or more decoding tags with the reporter mols., and detection of the decoding tags. The reporter mols. assoc. with target mols. in the target sample(s). Generally, the reporter mols. correspond to one or more target mols., and the decoding tags correspond to one or more reporter mols. Thus, detection of particular decoding tags indicates the presence of the corresponding reporter mols. In turn, the presence of particular reporter mols. indicates the presence of the corresponding target mols. The sensitivity of the disclosed method can also be enhanced by including a signal amplification step prior to detection. Medical applications of this method include the anal. of the phenotypic status or replicative status of cells (growth or quiescence) and the assessment of

normal and neoplastic cells in histol. or cytol. specimens in normal and disease states. For example, a pathologist may use the method to link a phenotypic state with the protein profile of lesion believed to contain malignant or pre-malignant cells.

IC ICM C12Q001-68
CC 9-16 (Biochemical Methods)
Section cross-reference(s): 3
IT Proteins, specific or class
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(DNA-binding; multiple tag anal.)
IT Protein motifs
(Helix-turn-helix; multiple tag anal.)
IT Proteins, specific or class
RL: ANT (Analyte); ANST (Analytical study)
(cell surface; multiple tag anal.)
IT Protein motifs
(leucine zipper; multiple tag anal.)
IT Proteins, specific or class
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(ligand-binding; multiple tag anal.)
IT ADP ribosylation
Adhesion, physical
Alkylation
Animal tissue
Bond cleavage
Cell
Cell division
Cell proliferation
Chromatography
Conformation
DNA sequences
Dimerization
Disease, animal
ESR spectroscopy
Electrophoresis
Fluorescent probes
Fluorometry
Fragmentation reaction
Glycosylation
HPLC
Immobilization, biochemical
Interface
Luminescence spectroscopy
Mass
Mass spectrometry
Methylation
Microwave
Molecular association
NMR spectroscopy
Neoplasm
Nucleic acid hybridization
Phenotypes
Phosphorimetry
Phosphorylation
Plates
Protein motifs
Ribosylation
SERS (Raman scattering)
Synthesis
(multiple tag anal.)

IT Carbohydrates, analysis
 DNA
 Peptides, analysis
 Prion proteins
 Receptors
 RL: ANT (Analyte); ANST (Analytical study)
 (multiple tag anal.)

IT Antibodies
 Haptens
Ligands
 Nucleic acid bases
 Oligonucleotides
 Peptide nucleic acids
 RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
 (multiple tag anal.)

IT Proteins, general, reactions
 RL: PRP (Properties); RCT (Reactant)
 (multiple tag anal.)

IT Conformation
 (protein; multiple tag anal.)

IT Molecules
 (target; multiple tag anal.)

IT Protein motifs
 (zinc finger; multiple tag anal.)

L24 ANSWER 17 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:756609 HCPLUS
 DOCUMENT NUMBER: 133:293180
 TITLE: The use of microfluidic systems in the electrochemical detection of target analytes
 INVENTOR(S): Kayyem, Jon Faiz
 PATENT ASSIGNEE(S): Clinical Micro Sensors, Inc., USA
 SOURCE: PCT Int. Appl., 119 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000062931	A1	20001026	WO 2000-US10903	20000421
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1183102	A1	20020306	EP 2000-923580	20000421
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			US 1999-295691	A 19990421
			WO 2000-US10903	W 20000421

AB The microfluidic system can comprise a solid support that has a sample inlet port, a first microchannel, a storage module (e.g., for assay reagents) and a second microchannel. The second microchannel may be in fluid contact directly with the detection module comprising a detection

electrode, or a self-assembled monolayer and a binding ligand. The device can contain a sample handling well and a second storage well with a microchannel leading to the sample handling well. The sample handling well could be a cell lysis chamber and the storage well could contain lysis reagents. The device can contain a sample handling well that is a cell capture or enrichment chamber, with an addnl. reagent storage well for elution buffer. The device may contain a reaction module with a storage module, e.g., for storage of amplification reagents. An optional waste module can be connected to the reaction module via a microchannel. The device may contain addnl. separators, valves, waste wells, and pumps, including addnl. electrodes. The microfluidic systems may be used for amplification and detection of nucleic acids, proteins or other biochem. analytes in biol. samples or cells.

IC ICM B01L003-00
 ICS C12Q001-68; G01N033-543
 CC 9-1 (Biochemical Methods)
 Section cross-reference(s): 3, 14, 76
 ST microfluidic system electrochem detection **target analyte**; nucleic acid electrochem detection microfluidic system; **protein** electrochem detection microfluidic system; diagnosis microfluidic system electrochem detection; lab chip electrochem detection **target analyte**
 IT DNA
 Nucleic acids
 Oligonucleotides
 Peptide nucleic acids
Proteins, general, analysis
 RNA
 mRNA
 rRNA
 RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
 (microfluidic systems for electrochem. detection of **target analytes**)
 IT **Ligands**
 RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL (Biological study); USES (Uses)
 (microfluidic systems for electrochem. detection of target analytes)
 IT **Probes** (nucleic acid)
 RL: BUU (Biological use, unclassified); DEV (Device component use); BIOL (Biological study); USES (Uses)
 (microfluidic systems for electrochem. detection of target analytes)
 REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 18 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:699119 HCAPLUS
 DOCUMENT NUMBER: 133:249316
 TITLE: Monolayer and electrode for detecting a label-bearing target and method of use thereof
 INVENTOR(S): Eckhardt, Allen E.; Mikulecky, Jill C.; Napier, Mary E.; Thomas, Robert S.; Thorp, H. Holden
 PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA; Xanthion, Inc.
 SOURCE: U.S., 21 pp., Cont.-in-part of U.S. Ser. No. 179,665.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 6
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6127127	A	20001003	US 1999-296929	19990422
US 5871918	A	19990216	US 1996-667338	19960620
US 5968745	A	19991019	US 1997-950503	19971014
US 6132971	A	20001017	US 1998-179665	19981027
WO 2000065099	A1	20001102	WO 2000-US2976	20000204
	W:	AE, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
EP 1185692	A1	20020313	EP 2000-913366	20000204
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO		

PRIORITY APPLN. INFO.:

US 1995-495817	B2	19950627
US 1996-667338	A3	19960620
US 1997-950503	A2	19971014
US 1998-179665	A2	19981027
US 1995-60949P	P	19950627
US 1996-16265P	P	19960419
US 1999-296929	A	19990422
WO 2000-US2976	W	20000204

AB An electrode for detecting interactions between members of a binding pair, which electrode has been modified by formation of a non-conductive self-assembled monolayer, and a method of detecting biomols., such as nucleic acids or other targets, including receptors, ligands, antigens or antibodies, utilizing such an electrode. When contacted with a target nucleic acid, an oligonucleotide probe coupled to the self-assembled monolayer reacts with the target nucleic acid to form a hybridized nucleic acid on the modified electrode surface. The hybridized nucleic acid is reacted with a transition metal complex capable of oxidizing a preselected base in the hybridized nucleic acid in an oxidn.-redn. reaction, the oxidn.-redn. reaction is detected, and the presence or absence of the nucleic acid is detd. from the detected oxidn.-redn. reaction.

IC ICM C12Q001-68
ICS C12M001-00; C07F009-22

NCL 435006000

CC 9-1 (Biochemical Methods)
Section cross-reference(s): 3, 15

IT Animal tissue culture
Biochemical molecules
Coupling agents
Diagnosis
Electrodes
Environmental analysis
Food analysis
Immobilization, biochemical
Monolayers
NASBA (nucleic acid sequence-based amplification)
Nucleic acid hybridization
Oxidation
PCR (polymerase chain reaction)
Redox reaction
Self-assembled monolayers

Surgery

Tooth

Veterinary medicine

(monolayer and electrode for detecting a label-bearing target and method of use thereof)

IT Antibodies

Antigens

Carbohydrates, analysis

Ligands

Nucleic acids

Proteins, general, analysis

Receptors

RL: ANT (Analyte); ANST (Analytical study)

(monolayer and electrode for detecting a label-bearing target and method of use thereof)

IT Probes (nucleic acid)

RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)

(monolayer and electrode for detecting a label-bearing target and method of use thereof)

IT Functional groups

(phosphonate group; monolayer and electrode for detecting a label-bearing target and method of use thereof)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 19 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:795994 HCPLUS

DOCUMENT NUMBER: 132:31744

TITLE: Gene probes used for genetic profiling in healthcare screening and planning

INVENTOR(S): Roberts, Gareth Wyn

PATENT ASSIGNEE(S): Genostic Pharma Ltd., UK

SOURCE: PCT Int. Appl., 745 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964627	A2	19991216	WO 1999-GB1780	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			GB 1998-12099	A 19980606
			GB 1998-13291	A 19980620
			GB 1998-13611	A 19980624
			GB 1998-13835	A 19980627
			GB 1998-14110	A 19980701
			GB 1998-14580	A 19980707
			GB 1998-15438	A 19980716
			GB 1998-15574	A 19980718

GB 1998-15576	A 19980718
GB 1998-16085	A 19980724
GB 1998-16086	A 19980724
GB 1998-16921	A 19980805
GB 1998-17097	A 19980807
GB 1998-17200	A 19980808
GB 1998-17632	A 19980814
GB 1998-17943	A 19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

IC ICM C12Q001-68

ICS C07K016-18

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 9, 13, 14

ST **probe** genetic profiling healthcare screening

IT Ankyrins

Calmodulins

Notch (receptor)

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(1 and 2 and 3, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT Angiotensin receptors

Fibrillins

Neurofibromin

Presenilins

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(1 and 2, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT Inositol 1,4,5-trisphosphate receptors

P-glycoproteins

Uncoupling protein

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 3, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Chloride channel**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 5 and KB, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Calbindins**

Keratins
Laminin receptors
Synaptobrevins
Syntaxins

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(10, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(11 and 2 and 3 and 9, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Interleukin receptors**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(12, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(13, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(14, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Myosins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(15 and 5A and 6 and 7A and cardiac, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(15, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(16, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(17, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Antigens**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(17-1A, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Keratins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(18, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Melatonin receptors**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(1A and 1B, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Tropomyosins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(1.alpha. and 3, core group of disease-related genes; gene **probes** used for **genetic** profiling in healthcare screening and planning)

IT **Calculi, renal**

(2, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT **Bone morphogenetic proteins**

Synaptobrevins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(2, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Bone morphogenetic proteins**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(2B, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Cyclin dependent kinase inhibitors**

(3, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Transcription factors**

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)

(3, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

IT **Keratins**

planning)

L24 ANSWER 20 OF 28 HCAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:795993 HCAPLUS
 DOCUMENT NUMBER: 132:31743
 TITLE: Gene probes used for genetic profiling in healthcare screening and planning
 INVENTOR(S): Roberts, Gareth Wyn
 PATENT ASSIGNEE(S): Genostic Pharma Limited, UK
 SOURCE: PCT Int. Appl., 149 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964626	A2	19991216	WO 1999-GB1779	19990604
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9941586	A1	19991230	AU 1999-41586	19990604
AU 9941587	A1	19991230	AU 1999-41587	19990604
GB 2339200	A1	20000119	GB 1999-12914	19990604
GB 2339200	B2	20010912		
EP 1084273	A1	20010321	EP 1999-925207	19990604
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			GB 1998-12098	A 19980606
			GB 1998-28289	A 19981223
			GB 1998-16086	A 19980724
			GB 1998-16921	A 19980805
			GB 1998-17097	A 19980807
			GB 1998-17200	A 19980808
			GB 1998-17632	A 19980814
			GB 1998-17943	A 19980819
			WO 1999-GB1779	W 19990604

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling

technologies.

IC ICM C12Q001-68
ICS C07K016-18

CC 3-1 (Biochemical Genetics)
Section cross-reference(s): 9, 13, 14

ST **probe** genetic profiling healthcare screening

IT Ankyrins
Calmodulins
Notch (receptor)
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 2 and 3, core group of **disease-related genes**; gene probes used for genetic profiling in healthcare screening and planning)

IT Angiotensin receptors
Fibrillins
Neurofibromin
Presenilins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 2, core group of **disease-related genes**; gene probes used for **genetic** profiling in healthcare screening and planning)

IT **Inositol** 1,4,5-trisphosphate receptors
P-glycoproteins
Uncoupling protein
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 3, core group of **disease-related genes**; gene probes used for genetic profiling in healthcare screening and planning)

IT **Chloride channel**
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1 and 5 and KB, core group of **disease-related genes**; gene probes used for genetic profiling in healthcare screening and planning)

IT Calbindins
Keratins
Laminin receptors
Synaptobrevins
Syntaxins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1, core group of **disease-related genes**; gene probes used for **genetic profiling** in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(10, core group of **disease-related genes**; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(11 and 2 and 3 and 9, core group of **disease-related genes**; gene probes used for genetic profiling in healthcare screening and planning)

IT **Interleukin** receptors

RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(12, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(13, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(14, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Myosins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(15 and 5A and 6 and 7A and cardiac, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(15, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(16, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(17, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Antigens
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(17-1A, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(18, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Melatonin receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1A and 1B, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Tropomyosins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(1.alpha. and 3, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

IT Calculi, renal
(2, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

- IT Bone morphogenetic proteins
Synaptobrevins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(2, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Bone morphogenetic proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(2B, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Cyclin dependent kinase inhibitors
(3, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Transcription factors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(3, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(4, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT Laminins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5, .alpha.3 and .beta.3 and .gamma.2, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1A, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1B, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1C, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1D, core group of disease-related genes; gene **probes** used for genetic profiling in healthcare screening and planning)

- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1E, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT1F, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT2A, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT2B, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT2C, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT3, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT4, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT5, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT6, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 5-HT receptors
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(5-HT7, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT **Bone morphogenetic proteins**
Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL

- (Biological study); USES (Uses)
(6, core group of disease-related genes; gene probes used for
genetic profiling in healthcare screening and planning)
- IT Bone morphogenetic proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(7, core group of disease-related genes; gene probes used for
genetic profiling in healthcare screening and planning)
- IT Bone morphogenetic proteins
Keratins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(8, core group of disease-related genes; gene
probes used for genetic profiling in healthcare
screening and planning)
- IT Apolipoproteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(A, A4, core group of disease-related genes; gene
probes used for genetic profiling in healthcare
screening and planning)
- IT Chromogranins
Cyclins
Glycophorins
Immunoglobulins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(A, core group of disease-related genes; gene probes
used for genetic profiling in healthcare
screening and planning)
- IT Apolipoproteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(A-I, core group of disease-related genes; gene probes used
for genetic profiling in healthcare screening and planning)
- IT Apolipoproteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(A-II, core group of disease-related genes; gene probes used
for genetic profiling in healthcare screening and planning)
- IT Heat-shock proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(A1 and A2, core group of disease-related genes; gene probes
used for genetic profiling in healthcare screening and planning)
- IT Transport proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(ABC (ATP-binding cassette-contg.), 7, core group of disease-
related genes; gene probes used for genetic profiling
in healthcare screening and planning)
- IT Proteins, specific or class
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL
(Biological study); USES (Uses)
(ABP (androgen-binding protein), core group of
disease-related genes; gene probes used for genetic
profiling in healthcare screening and planning)
- IT Transport proteins
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL

- used for genetic profiling in healthcare screening and planning)
IT 9025-75-6, Protein phosphatase
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(regulatory subunit PPP1R3 and A, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 9001-78-9
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(tissue nonspecific TNSAP, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 79747-53-8, Protein tyrosine phosphatase
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(type 12, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 158736-49-3, .alpha.-Secretase
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.alpha. and .beta. and .gamma., core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 57285-09-3, Inhibin
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.alpha. and .beta.A and .beta.B and .beta.C subunits, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)
- IT 9002-67-9, Luteinizing hormone
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(.beta.-subunit, core group of disease-related genes; gene probes used for genetic profiling in healthcare screening and planning)

L24 ANSWER 21 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:454278 HCPLUS
DOCUMENT NUMBER: 131:85125
TITLE: Method and device comprising capture molecule fixed on disc surface
INVENTOR(S): Remacle, Jose
PATENT ASSIGNEE(S): Belg.
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9935499	A1	19990715	WO 1998-BE206	19981224
W:	AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, DE, DE, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,			

CM, GA; GN, GW, ML, MR, NE, SN, TD, TG			
CA 2312173	AA 19990715	CA 1998-2312173	19981224
AU 9920418	A1 19990726	AU 1999-20418	19981224
BR 9814726	A 20001017	BR 1998-14726	19981224
EP 1044375	A1 20001018	EP 1998-965057	19981224
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI			
JP 2002501174 T2 20020115		JP 2000-527830	19981224
PRIORITY APPLN. INFO.:		US 1997-71726P	P 19971230
		WO 1998-BE206	W 19981224

- AB The present invention is related to a method for the detection and/or the quantification of a target mol. by its binding with a non-cleavable capture mol. fixed on the surface of a disk comprising registered data. The present invention is also related to a disk having fixed upon its surface a non-cleavable capture mol., to its prepn. process, and to a diagnostic and/or reading device of said disk or comprising said disk. Cytomegalovirus and HIV DNA and bovine serum albumin were detected on compact disks (CDs). For DNA detection, capture probes were bound to aminated polycarbonate CDs. For protein detection, antibodies were fixed on a carboxylated CD. Detection involved using biotinylated DNA or antibodies, streptavidin-peroxidase, and TMB to give a blue color.
- IC ICM G01N033-543
ICS C12Q001-68
- CC 9-1 (Biochemical Methods)
Section cross-reference(s): 3, 10, 15, 73, 74, 80
- IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(aminated polycarbonate compact disk-immobilized, for DNA detection; method and device comprising capture mol. fixed on disk surface)
- IT Polycarbonates, uses
RL: ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(aminated, compact disk of, capture probe immobilized on, for DNA detection; method and device comprising capture mol. fixed on disk surface)
- IT Catalysts
Chromophores
Fluorescent substances
(as capture or target mol.; method and device comprising capture mol. fixed on disk surface)
- IT Antibodies
Antigens
Carbohydrates, analysis
Haptens
Ligands
Lipids, analysis
Peptides, analysis
Proteins, general, analysis
Receptors
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(as capture or target mol.; method and device comprising capture mol. fixed on disk surface)
- IT Nucleic acids
RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(as capture or target mol.; method and device comprising capture mol. fixed on disk surface)
- IT Cytomegalovirus
Human immunodeficiency virus

(capture probe of, immobilization of, on aminated polycarbonate compact disk; method and device comprising capture mol. fixed on disk surface)

IT Precipitates
(detection of formation of, in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

IT DNA
RL: ANT (Analyte); ANST (Analytical study)
(detection of, by aminated polycarbonate compact disk-immobilized capture probe; method and device comprising capture mol. fixed on disk surface)

IT Immunoassay
(enzyme-linked immunosorbent assay, bovine serum albumin detection by, on compact disk; method and device comprising capture mol. fixed on disk surface)

IT Magnetic particles
(in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

IT Colloids
(metals, detection of formation of, in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

IT Combinatorial chemistry
(new macromols. obtained by, as capture or target mol.; method and device comprising capture mol. fixed on disk surface)

IT Macromolecular compounds
RL: ANT (Analyte); ARG (Analytical reagent use); DEV (Device component use); ANST (Analytical study); USES (Uses)
(obtained by combinatorial chem., as capture or target mol.; method and device comprising capture mol. fixed on disk surface)

IT Corrosion
(of layer on disk surface, in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

IT Metals, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(ppts., detection of formation of, in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

IT 7440-22-4, Silver, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(ppts., detection of formation of, in detection of binding of target and capture mols.; method and device comprising capture mol. fixed on disk surface)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 22 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:317213 HCPLUS
DOCUMENT NUMBER: 130:335007
TITLE: Extended dynamic range assays using at least two labeled probes for different target regions on an analyte
INVENTOR(S): Nelson, Norman C.
PATENT ASSIGNEE(S): Gen-Probe Incorporated, USA
SOURCE: PCT Int. Appl., 55 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9923490	A1	19990514	WO 1998-US23088	19981030
W: AU, CA, JP, KR RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6180340	B1	20010130	US 1997-962033	19971031
AU 9912918	A1	19990524	AU 1999-12918	19981030
AU 741568	B2	20011206		
EP 1027604	A1	20000816	EP 1998-956381	19981030
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, LU, NL, SE				
US 6350579	B1	20020226	US 2000-649636	20000828
PRIORITY APPLN. INFO.:			US 1997-962033 A	19971031
			WO 1998-US23088 W	19981030

AB Methods of detecting and/or quantifying an analyte in a single sample by using at least two labeled probes that specifically bind to different target regions of an analyte, and are labeled with labels that are distinguishable and/or present at different specific activities, are disclosed. Compns. comprising at least two labeled probes that specifically bind to different target regions of the same analyte and are labeled with labels that are distinguishable and/or present at different specific activities are disclosed. 1-Methyl-m-difluoroacridinium ester, 1-methylacridinium ester, and o-methoxy(cinnamyl)acridinium ester were shown to be distinguishable under conditions that replicate those of analyte detection using chemiluminescence. The three labels were used at a specific activity of 108, 106, and 104, resp.

IC ICM G01N033-543

ICS G01N033-53; G01N033-58; C12Q001-68

CC 9-5 (Biochemical Methods)

Section cross-reference(s): 3

IT DNA

RNA

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(analogs, as **probe**; extended dynamic range assays using at least two labeled **probes** for different target regions on an analyte)

IT Carbohydrates, analysis

Lipids, analysis

Nucleic acids

Proteins (general), analysis

RNA

RL: ANT (Analyte); ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(as analyte or **probe**; extended dynamic range assays using at least two labeled **probes** for different **target** regions on an analyte)

IT Chemiluminescent substances

Chromophores

Fluorescent substances

Luminescent substances

Radioactive substances

(as detectable label; extended dynamic range assays using at least two labeled **probes** for different target regions on an analyte)

IT DNA

IT RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(as probe; extended dynamic range assays using at least two
labeled probes for different target regions on an analyte)

IT Ligands
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(binding signal-producing binding partner, as detectable label;
extended dynamic range assays using at least two labeled probes
for different target regions on an analyte)

IT Analysis
Chemiluminescence spectroscopy
Fluorometry
Luminescence spectroscopy
Nucleic acid hybridization
Radiochemical analysis
Spectroscopy
(extended dynamic range assays using at least two labeled
probes for different target regions on an analyte)

IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(extended dynamic range assays using at least two labeled
probes for different target regions on an analyte)

IT Reaction kinetics
(labeled probes distinguishable by; extended dynamic range
assays using at least two labeled probes for different target
regions on an analyte)

IT Reagents
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(labeled probes; extended dynamic range assays using at least
two labeled probes for different target regions on an
analyte)

IT Enzymes, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(or enzyme substrates, as detectable label; extended dynamic
range assays using at least two labeled probes for different
target regions on an analyte)

IT 22559-71-3D, Acridinium, ester derivs.
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(as detectable label; extended dynamic range assays using at least two
labeled probes for different target regions on an analyte)

IT 224169-61-3 224169-63-5 224169-64-6
RL: ARG (Analytical reagent use); PRP (Properties); ANST (Analytical
study); USES (Uses)
(as detectable label; extended dynamic range assays using at least two
labeled probes for different target regions on an analyte)

IT 224169-65-7DP, conjugates with oligonucleotide probe
224169-66-8DP, conjugates with oligonucleotide probe
224169-67-9DP, conjugates with oligonucleotide probe
RL: ARG (Analytical reagent use); PRP (Properties); SPN (Synthetic
preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
(for synthetic RNA oligomer detn.; extended dynamic range assays using
at least two labeled probes for different target regions on
an analyte)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 23 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:34437 HCAPLUS
DOCUMENT NUMBER: 130:107243
TITLE: Methods of detection using a cellulose binding domain
fusion product

INVENTOR(S): Shoseyov, Oded; Shpiegl, Itai; Goldstein, Marc A.;
Doi, Roy H.

PATENT ASSIGNEE(S): Yissum Research Development Company of the Hebrew University of Jerusalem, Israel; The University of California

SOURCE: U.S., 63 pp., Cont.-in-part of U.S. 5,496,934.

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5856201	A	19990105	US 1994-330394	19941027
US 5496934	A	19960305	US 1993-48164	19930414
CA 2160670	AA	19941027	CA 1994-2160670	19940414
CN 1125452	A	19960626	CN 1994-192440	19940414
CN 1059214	B	20001206		
US 5670623	A	19970923	US 1995-460462	19950602
US 5719044	A	19980217	US 1995-460457	19950602
US 5738984	A	19980414	US 1995-460458	19950602
US 5837814	A	19981117	US 1995-460455	19950602
CN 1217339	A	19990526	CN 1998-118445	19980813
CN 1223377	A	19990721	CN 1998-118443	19980813

PRIORITY APPLN. INFO.: US 1993-48164 A2 19930414

AB A cellulose binding domain (CBD) having a high affinity for cryst. cellulose and chitin is disclosed, along with methods for the mol. cloning and recombinant prodn. thereof. Fusion products comprising the CBD and a second protein (binding to target substances) are likewise described. The fusion products are useful in detecting target substances. IgG was purified from human serum using recombinantly-prepd. CBD-protein A fusion product bound to cellulose.

IC ICM G01N033-52

ICS G01N033-58; G01N033-68

NCL 436501000

CC 9-2 (Biochemical Methods)

Section cross-reference(s): 3, 15

ST cellulose binding domain **protein** analysis; IgG purifn
cellulose binding domain **protein** A

IT Serum (blood)

(IgG of human purifn. from, by cellulose binding domain-**protein**
A cellulose; methods of detection using cellulose binding domain fusion
products)

IT Escherichia coli

(cellulose binding domain **protein** and fusion products
expression in; methods of detection using cellulose binding domain
fusion products)

IT **Proteins** (specific **proteins** and subclasses)

RL: ARG (Analytical reagent use); BPR (Biological process); ANST
(Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(cellulose-binding domain, fusion products with **proteins**
binding **target** substances; methods of detection using
cellulose binding domain fusion products)

IT Chimeric genes

RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)

(for fusion **proteins** contg. cellulose binding domain; methods
of detection using cellulose binding domain fusion products)

IT **Protein** A

RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR (Biological process); BUU (Biological use, unclassified); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(fusion products with cellulose binding domain **protein**;
methods of detection using cellulose binding domain fusion products)

IT Antibodies
RL: ARG (Analytical reagent use); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(fusion products with cellulose binding domain **protein**;
methods of detection using cellulose binding domain fusion products)

IT PCR (polymerase chain reaction)
(in prepn. of cellulose binding domain **protein** fusion
products; methods of detection using cellulose binding domain fusion
products)

IT Proteins (specific proteins and subclasses)
RL: ARG (Analytical reagent use); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(ligand-binding, fusion products with cellulose-binding
domain **protein**; methods of detection using cellulose binding
domain fusion products)

IT Antibodies
Hormones (animal), analysis
Nucleic acids
Peptides, analysis
Proteins (general), analysis
RL: ANT (Analyte); ANST (Analytical study)
(methods of detection using cellulose binding domain fusion products)

IT Fusion proteins (chimeric proteins)
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR (Biological process); ANST (Analytical study); BIOL (Biological study);
PREP (Preparation); PROC (Process); USES (Uses)
(of cellulose-binding domain **protein** and **proteins**
binding target substances; methods of detection using
cellulose binding domain fusion products)

IT Enzymes, uses
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(or substrate or cofactor or inhibitor of, as label; methods of
detection using cellulose binding domain fusion products)

IT Protein HSP60
RL: BPN (Biosynthetic preparation); BPR (Biological process); BIOL (Biological study); PREP (Preparation); PROC (Process)
(peptide of, fusion products with cellulose binding domain
protein; methods of detection using cellulose binding domain
fusion products)

IT IgG
RL: BPR (Biological process); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation); PROC (Process)
(purifn. of, by cellulose binding domain-**protein** A cellulose;
methods of detection using cellulose binding domain fusion products).

IT 506-68-3, Cyanogen bromide ((CN)Br)
RL: NUU (Other use, unclassified); USES (Uses)
(HSP60 peptide fusion product with cellulose binding domain
protein cleavage with; methods of detection using cellulose
binding domain fusion products)

IT 133554-23-1DP, fusion products with cellulose binding domain
protein CBD1
RL: BPN (Biosynthetic preparation); PRP (Properties); RCT (Reactant); BIOL (Biological study); PREP (Preparation)
(amino acid sequence, cyanogen bromide cleavage of; methods of

detection using cellulose binding domain fusion products)
IT 160478-79-5DP, 28-189-Protein CbpA (*Clostridium cellulovorans* clone pCB1 gene cbpA cellulose-binding precursor reduced), fusion products with **proteins** binding **target** substances
219591-04-5DP, fusion products with **proteins** binding **target** substances 219591-05-6DP, fusion products with **proteins** binding **target** substances
RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR (Biological process); PRP (Properties); PUR (Purification or recovery); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(amino acid sequence; methods of detection using cellulose binding domain fusion products)
IT 9003-99-0D, Peroxidase, fusion products with cellulose binding domain **protein**
RL: ARG (Analytical reagent use); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(horseradish; methods of detection using cellulose binding domain fusion products)
IT 58-85-5D, Biotin, conjugates with **probe** bound to targetable mol.
RL: ANT (Analyte); ANST (Analytical study)
(methods of detection using cellulose binding domain fusion products)
IT 1398-61-4, Chitin 9001-78-9D, fusion products with cellulose binding domain **protein** 9013-20-1D, Streptavidin, fusion products with cellulose binding domain **protein**
RL: ARG (Analytical reagent use); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(methods of detection using cellulose binding domain fusion products)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 24 OF 28 HCPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:8005 HCPLUS
DOCUMENT NUMBER: 130:77958
TITLE: sequence and development-specific activity of Cdc2
protein kinase from *Pneumocystis carinii* and
methods for mutation screening for clinical diagnosis
INVENTOR(S): Limper, Andrew H.; Leof, Edward B.; Thomas, Charles
F.; Gustafson, Michael P.
PATENT ASSIGNEE(S): Mayo Foundation for Medical Education and Research,
USA
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9856799	A1	19981217	WO 1998-US12100	19980612
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5863741	A	19990126	US 1997-874347	19970613
US 6015700	A	20000118	US 1998-93522	19980608
PRIORITY APPLN. INFO.:			US 1997-874347	19970613
AB A nucleic acid and corresponding polypeptide that aids in the regulation of the cell cycle in <i>Pneumocystis carinii</i> is described. Antibodies generated against a unique carboxyl-terminus region of the polypeptide have specific binding affinity for <i>P. carinii</i> Cdc2 polypeptide and are				

beneficial in diagnosing and monitoring *P. carinii* infection in patients. Expression of *P. carinii* Cdc2 polypeptide in cdc2-mutant yeast and other cdc-mutant organisms provides a useful model for studying the life cycle of *P. carinii* and for identifying novel therapeutics.

IC ICM C07H017-00

ICS C12N005-00; C12N015-00; C07K014-00; C12Q001-00; C12Q001-68

CC 7-2 (Enzymes)

Section cross-reference(s): 3, 10

IT Cyclins

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (B, phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Nucleic acid hybridization

(DNA-DNA; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Histones

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (H1, phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Transcription factors

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (Rb, phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT PCR (polymerase chain reaction)

(diagnosis involving; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Genetic vectors

Schizosaccharomyces pombe (expression host *Schizosaccharomyces pombe* expression vector; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT *Saccharomyces cerevisiae*

(expression host; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Proteins, specific or class

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (gene CDC25, phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)

IT Proteins, specific or class

RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study) (gene cdc25, phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from *Pneumocystis carinii* and methods for

- mutation screening for clin. diagnosis)
- IT Animal tissue
- Body fluid
(infection diagnosis in; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Infection
(method for diagnosis of; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Antibodies
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(monoclonal, specific for C-terminal domain; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Proteins, specific or class
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(nuclear lamin-assocd.; phosphorylation **target** for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Phosphorylation, biological
(**protein**, method for detection of phosphorylation activity inhibition; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Cell cycle
- DNA sequences
- Epitopes
- Pneumocystis carinii*
- Protein** sequences
- cDNA sequences
(sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Probes (nucleic acid)
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(sequence and development-specific **activity** of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT Development, microbial
(trophozoite; high Cdc2 kinase activity during; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT 218269-64-8
RL: ANT (Analyte); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(amino acid sequence of epitope specific for monoclonal antibody; sequence and development-specific activity of Cdc2 **protein** kinase from *Pneumocystis carinii* and methods for mutation screening for clin. diagnosis)
- IT 206010-93-7, Kinase (phosphorylating), gene cdc2 **protein**
(*Pneumocystis carinii*)

Tran 09/738,954

RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; sequence and development-specific activity of Cdc2 protein kinase from Pneumocystis carinii and methods for mutation screening for clin. diagnosis)

- IT 199151-54-7 218438-99-4
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; sequence and development-specific activity of Cdc2 protein kinase from Pneumocystis carinii and methods for mutation screening for clin. diagnosis)
- IT 143375-65-9, Cdc2 protein kinase
RL: BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sequence and development-specific activity of Cdc2 protein kinase from Pneumocystis carinii and methods for mutation screening for clin. diagnosis)
- IT 9012-90-2
RL: ARU (Analytical role, unclassified); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(.alpha., .alpha., .alpha.; phosphorylation target for Cdc2 kinase indicating functionality; sequence and development-specific activity of Cdc2 protein kinase from Pneumocystis carinii and methods for mutation screening for clin. diagnosis)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 25 OF 28 HCAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:106052 HCAPLUS
DOCUMENT NUMBER: 128:163644
TITLE: A homogeneous nucleic acid detection method utilizing simultaneous target and signal amplification
INVENTOR(S): Hepp, Jozsef; Lengyel, Zsolt; Pande, Rajiv;
Botyanszki, Janos; Sahin-Toth, Miklos
PATENT ASSIGNEE(S): Navix, Inc., USA; Hepp, Jozsef; Lengyel, Zsolt; Pande,
Rajiv; Botyanszki, Janos; Sahin-Toth, Miklos
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804739	A2	19980205	WO 1997-US12415	19970716
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5858665	A	19990112	US 1996-692825	19960725
AU 9736668	A1	19980220	AU 1997-36668	19970716
AU 728416	B2	20010111		
EP 918883	A2	19990602	EP 1997-933502	19970716
R: BE, CH, DE, FR, GB, IT, LI, NL, SE, IE				
PRIORITY APPLN. INFO.:		US 1996-692825	A	19960725

AB A method for detg. the presence of a target nucleic acid in a sample using a two-stage target cycling reaction is described. The method uses a hybridization probe that is complexed with an activator. When the probe hybridizes with its target the activator is released. The activator then interacts with an analog of the target sequence that is immobilized via an anchor moiety, leading to its release and the generation of a signal specific to the released cleavage products. The released target analog then restarts the cyclic reaction by binding to a second probe, which effectuates release of a second activator, and so on. This cyclic reaction amplifies the signal generated from a single target nucleic acid mol. in the sample, which greatly enhances the level of target detection that can be expected. The analog and the target have to be sepd. in the assay and this can be brought about by immobilizing them on sep. surfaces or using a membrane that is permeable to the released activator and target analog, but not the target or the free probe. An enzyme-based version of the assay is demonstrated. An oligonucleotide probe with a central oligoribonucleotide was prep., conjugated with enterokinase, and immobilized. The anchored target analog was conjugated to trypsinogen. When the target sequence hybridizes to the enterokinase labeled probe, it is cleaved at the RNA moiety with RNase H to release the enterokinase. The released enterokinase cleaves the trypsinogen to release the oligonucleotide. The resulting trypsin can be assayed with a chromogenic substrate.

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)

Section cross-reference(s): 9

ST target cycling reaction hybridization amplification; **probe**
conjugate cleavage activation signal amplification; enterokinase
probe conjugate signal amplification; trypsinogen activation
signal amplification

IT **Functional groups**

(guanidino group, stabilization of **proteins** using;
homogeneous nucleic acid detection method utilizing simultaneous
target and signal amplification)

IT Polysaccharides, analysis

RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(immobilized conjugates with oligonucleotides, **enzymic**
hydrolysis in signal generation and amplification; homogeneous nucleic
acid detection method utilizing simultaneous target and signal
amplification)

IT **Probes** (nucleic acid)

RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(mixed compn., conjugates; homogeneous nucleic acid detection method
utilizing simultaneous target and signal amplification)

IT Polyoxalkylenes, uses

RL: NUU (Other use, unclassified); USES (Uses)
(stabilization of **proteins** using; homogeneous nucleic acid
detection method utilizing simultaneous **target** and signal
amplification)

IT 9001-92-7D, Proteinase, conjugates with hybridization **probes**

9014-74-8D, Enterokinase, conjugates with hybridization **probes**

RL: ARG (Analytical reagent use); CAT (Catalyst use); ANST (Analytical
study); USES (Uses)
(in signal generation and amplification; homogeneous nucleic acid
detection method utilizing simultaneous target and signal
amplification)

IT 25322-68-3, Polyethylene glycol

RL: NUU (Other use, unclassified); USES (Uses)
(stabilization of **proteins** using; homogeneous nucleic acid

detection method utilizing simultaneous target and signal amplification)

L24 ANSWER 26 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:294518 HCPLUS
 DOCUMENT NUMBER: 126:273240
 TITLE: Nucleic acid reactions under isothermal conditions where a probe-target nucleic acid duplex reacts with an enzyme and single-strand-binding ligand facilitates thermodynamic cycling of the system
 INVENTOR(S): Lane, Michael J.; Benight, Albert S.; Faldasz, Brian D.
 PATENT ASSIGNEE(S): Lane, Michael J., USA; Benight, Albert S.; Faldasz, Brian D.
 SOURCE: PCT Int. Appl., 83 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9711199	A1	19970327	WO 1996-US15199	19960923
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
AU 9673685	A1	19970409	AU 1996-73685	19960923
PRIORITY APPLN. INFO.:			US 1995-532310	19950922
			US 1996-635067	19960419
			WO 1996-US15199	19960923

AB This invention describes thermodn. cycling reaction methods for a single-stranded target nucleic acid which has bound by a single-stranded probe nucleic acid and its reaction with an enzyme such as Taq polymerase, DNA ligase, or RNaseH. The reaction mixt. comprises a plurality of single-stranded nucleic acid probes, at least one single-stranded nucleic acid target, a single-strand-binding ligand to facilitate thermodn. cycling of the system and an enzyme such as RNaseH which has the chem. potential of the single-strand-binding ligand. The thermodn. cycling reaction occurs under isothermal conditions. Reaction steps include (a) the formation of a probe-target nucleic acid duplex (b) a reaction between the enzyme and the first formed duplex, (c) the dissoln. of the first formed duplex, (d) the formation of a second duplex between a subsequent probe and target and (e) a reaction between the enzyme and the second formed duplex. The reaction cycles at least at least 1 time, and may cycle 2, 5, 10, 25, 50, 100, 500, 103, 104, 105, or 106 times. Examples of applications of the method include isothermal PCR and improved ligase chain reactions.

IC ICM C12Q001-68

CC 3-1 (Biochemical Genetics)

ST nucleic acid reaction isothermal thermodn cycling; amplification nucleic acid isothermal thermodn cycling; RNaseH nucleic acid reaction thermodn cycling; PCR isothermal thermodn cycling reaction; ligase chain reaction thermodn cycling reaction; single strand binding ligand thermodn cycling

IT Chemical potential

(**enzyme** and single-strand binding **ligand**; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT PCR (polymerase chain reaction)

(isothermal; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Genetic methods

(ligase chain reaction; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Nucleic acid amplification (method)

Thermodynamics

(nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Enzymes, properties

RL: CAT (Catalyst use); PRP (Properties); USES (Uses)
(nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Protein SSB

RL: MOA (Modifier or additive use); PRP (Properties); USES (Uses)
(nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Nucleic acids

RL: RCT (Reactant)
(nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Oligonucleotides

RL: NUU (Other use, unclassified); USES (Uses)
(**probes**; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT Ligands

RL: MOA (Modifier or additive use); PRP (Properties); USES (Uses)
(single-strand-binding; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT 9012-90-2, DNA polymerase

RL: CAT (Catalyst use); PRP (Properties); USES (Uses)
(Taq; nucleic acid reactions under isothermal conditions where **probe-target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

IT 9015-85-4, DNA ligase 9050-76-4, RNaseH 63774-49-2, RNase H*

RL: CAT (Catalyst use); PRP (Properties); USES (Uses)

(nucleic acid reactions under isothermal conditions where **probe**-**target** nucleic acid duplex reacts with **enzyme** and single-strand-binding **ligand** facilitates thermodn. cycling of system)

L24 ANSWER 27 OF 28 HCPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:576736 HCPLUS
 DOCUMENT NUMBER: 115:176736
 TITLE: Amplification capture assay
 INVENTOR(S): Brakel, Christine L.; Spadoro, Joanne P.
 PATENT ASSIGNEE(S): Enzo Biochem, Inc., USA
 SOURCE: Eur. Pat. Appl., 40 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 435150	A2	19910703	EP 1990-124738	19901219
EP 435150	A3	19920129		
R: DE, ES, FR, GB, IT				
CA 2032203	AA	19910630	CA 1990-2032203	19901213
EP 1113082	A2	20010704	EP 2000-126204	19901219
R: DE, ES, FR, GB, IT				
JP 04141099	A2	19920514	JP 1990-418011	19901228
JP 2000325093	A2	20001128	JP 2000-118781	19901228
PRIORITY APPLN. INFO.:			US 1989-459030 A	19891229
			EP 1990-124738 A3	19901219
			JP 1990-418011 A3	19901228

AB A method for detecting single-stranded nucleic acids in a sample based on nucleic acid amplification and use of a matrix-bound oligonucleotide and an oligonucleotide-label capturing moiety conjugate is described. The method is adaptable to high vol. and clin. testing, e.g. it is adaptable to automation. Addnl., it can be modified to provide ests. of the efficiency of amplification. The process comprises (1) amplification of the target nucleic acid; (2) contacting the amplified nucleic acid with a target-specific hybridization probe attached to a label-capturing moiety (such as biotin or streptavidin); (3) contacting the amplified nucleic acid with a matrix-attached 2nd oligonucleotide hybridization probe specific for the target; (4) sepg., if necessary, the bound complex from unbound nucleic acid; and (45) detg. the presence or absence of the amplified target nucleic acid by capturing and observing the presence or absence of the label (e.g. with a biotin- or streptavidin-enzyme complex). Alternatively, the target nucleic acid can first be captured with a matrix-oligonucleotide conjugate and sepd. from unbound nucleic acids. Using this method, as little as 1 copy of HIV/1.5 times 10⁵ peripheral blood cells could be detected.

IC ICM C12Q001-68
 ICS C07H021-04; C12Q001-70

CC 3-5 (Biochemical Genetics)

IT Agglutinins and Lectins

Antibodies

Antigens

Hormones

Receptors

RL: BIOL (Biological study)

(oligonucleotide hybridization **probe** conjugates, in detection of amplified target nucleic acids, capture **probes** in relation

to)

IT Virus, animal
 (Epstein-Barr, detection of, nucleic acid amplification and oligonucleotide **probe** conjugates in)

IT Enzymes
 RL: BIOL (Biological study)
 (apo-, conjugates, with oligonucleotide hybridization **probes**, in detection of amplified target nucleic acids, capture **probes** in relation to)

IT Avidins
 RL: BIOL (Biological study)
 (conjugates, with oligonucleotide hybridization **probe**, in detection of amplified target nucleic acids, capture **probes** in relation to)

IT Carbohydrates and Sugars, compounds
 Coenzymes
 RL: BIOL (Biological study)
 (conjugates, with oligonucleotide hybridization **probes**, in detection of amplified target nucleic acids, capture **probes** in relation to)

IT Virus, animal
 (human immunodeficiency 1, detection of, nucleic acid amplification and oligonucleotide **probe** conjugates in)

IT Nucleotides, polymers
 RL: BIOL (Biological study)
 (oligo-, conjugates, with matrix, with ligand or receptor, in detection of nucleic acids, nucleic acid amplification in relation to)

IT 58-85-5D, Biotin, conjugate with oligonucleotide hybridization **probe**
 9013-20-1D, Streptavidin, conjugate with oligonucleotide hybridization **probe**
 RL: PRP (Properties)
 (in detection of amplified target nucleic acids, capture **probes** in relation to)

IT 9012-90-2, DNA polymerase
 RL: BIOL (Biological study)
 (nucleic acid amplification with, in detection of target nucleic acid, capture **probes** in relation to)

IT 9026-28-2, Q.beta. Replicase 9068-38-6, Reverse transcriptase
 RL: PRP (Properties)
 (nucleic acid amplification with, in detection of target nucleic acid, capture **probes** in relation to)

IT 136541-95-2 136541-96-3
 RL: PRP (Properties)
 (oligonucleotide **probe** for detection of amplified Epstein-Barr virus sequence)

IT 136542-08-0 136542-09-1
 RL: PRP (Properties)
 (oligonucleotide **probe** for detection of amplified HIV sequence)

L24 ANSWER 28 OF 28 HCPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:229742 HCPLUS

DOCUMENT NUMBER: 112:229742

TITLE: DNA and RNA molecules stabilized by modifications of the 3'-terminal phosphodiester linkage and their use as nucleic acid **probes** and as therapeutic agents to block the expression of specifically targeted genes

INVENTOR(S): Walder, Joseph A.; Walder, Roxanne Y.; Eder, Paul S.; Dagle, John M.

PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA
 SOURCE: PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8905358	A1	19890615	WO 1988-US3842	19881031
W: AU, JP				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8927829	A1	19890705	AU 1989-27829	19881031
AU 620364	B2	19920220		
EP 348458	A1	19900103	EP 1988-910300	19881031
EP 348458	B1	19970409		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502516	T2	19900816	JP 1988-509389	19881031
JP 3019994	B2	20000315		
AT 151467	E	19970415	AT 1988-910300	19881031
CA 1339935	A1	19980630	CA 1988-582338	19881104
US 5491133	A	19960213	US 1991-672088	19910319
US 5403711	A	19950404	US 1993-88622	19930706
US 6197944	B1	20010306	US 1994-268381	19940629
US 5962425	A	19991005	US 1995-460704	19950602
PRIORITY APPLN. INFO.:			US 1987-126564	A 19871130
			US 1988-173127	B1 19880324
			WO 1988-US3842	A 19881031
			US 1991-672088	A3 19910319
			US 1991-757555	B1 19910911

- AB The invention comprises the method, means, and compn. which together enable the use of oligonucleotides that are modified at the 3'-terminal phosphodiester linkage, and are thereby rendered resistant to degrdn. within cells and body fluids, to selectively block the expression of a particular gene. The method involves the hybridization of the modified oligonucleotide to the corresponding mRNA to form a substrate fully capable of being recognized by the enzyme RNaseH, followed by the cleavage of the mRNA at the site of the RNA-DNA double helix such that the expression of the targeted gene is blocked. The invention further details the use of DNA and RNA mols. modified at the 3'-terminal phosphodiester linkage as nucleic acid probes for diagnostic applications. Anti-c-myc oncogene oligonucleotide, 5'-GXTAGGGAAAGACCACTGAGGGT_XC [X = trichlorodimethylphosphotriester (incorporation method described)], at 1 .mu.M, decreased the level of c-myc mRNA in MOPC 315 cells by 75% compared to the steady-state level of the mRNA in MOPC 315 cells incubated in the absence of the oligonucleotide.
- IC C12Q001-68; C07H211-00
- CC 1-12 (Pharmacology)
- ST Section cross-reference(s): 3, 9, 33
- phosphodiester modification DNA stabilization; RNA stabilization phosphodiester modification; nucleic acid stabilization phosphodiester modification; oligonucleotide probe nuclease resistance; gene expression blockage phosphodiester modification
- IT Protein formation
 (inhibition of, modified oligonucleotides to target mRNA in)
- IT Diagnosis
- Nucleic acid hybridization
 (nuclease-resistant oligonucleotide probes for)
- IT Functional groups

PATENT ASSIGNEE(S): University of Iowa Research Foundation, USA
 SOURCE: PCT Int. Appl., 50 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8905358	A1	19890615	WO 1988-US3842	19881031
W: AU, JP RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
AU 8927829	A1	19890705	AU 1989-27829	19881031
AU 620364	B2	19920220		
EP 348458	A1	19900103	EP 1988-910300	19881031
EP 348458	B1	19970409		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
JP 02502516	T2	19900816	JP 1988-509389	19881031
JP 3019994	B2	20000315		
AT 151467	E	19970415	AT 1988-910300	19881031
CA 1339935	A1	19980630	CA 1988-582338	19881104
US 5491133	A	19960213	US 1991-672088	19910319
US 5403711	A	19950404	US 1993-88622	19930706
US 6197944	B1	20010306	US 1994-268381	19940629
US 5962425	A	19991005	US 1995-460704	19950602
PRIORITY APPLN. INFO.:			US 1987-126564	A 19871130
			US 1988-173127	B1 19880324
			WO 1988-US3842	A 19881031
			US 1991-672088	A3 19910319
			US 1991-757555	B1 19910911

- AB The invention comprises the method, means, and compn. which together enable the use of oligonucleotides that are modified at the 3'-terminal phosphodiester linkage, and are thereby rendered resistant to degrdn. within cells and body fluids, to selectively block the expression of a particular gene. The method involves the hybridization of the modified oligonucleotide to the corresponding mRNA to form a substrate fully capable of being recognized by the enzyme RNaseH, followed by the cleavage of the mRNA at the site of the RNA-DNA double helix such that the expression of the targeted gene is blocked. The invention further details the use of DNA and RNA mols. modified at the 3'-terminal phosphodiester linkage as nucleic acid probes for diagnostic applications. Anti-c-myc oncogene oligonucleotide, 5'-GXTAGGGAAAGACCACTGAGGGTGC [X = trichlorodimethylphosphotriester (incorporation method described)], at 1 .mu.M, decreased the level of c-myc mRNA in MOPC 315 cells by 75% compared to the steady-state level of the mRNA in MOPC 315 cells incubated in the absence of the oligonucleotide.
- IC C12Q001-68; C07H211-00
- CC 1-12 (Pharmacology)
 Section cross-reference(s): 3, 9, 33
- ST phosphodiester modification DNA stabilization; RNA stabilization phosphodiester modification; nucleic acid stabilization phosphodiester modification; oligonucleotide **probe** nuclease resistance; gene expression blockage phosphodiester modification
- IT **Protein formation**
 (inhibition of, modified oligonucleotides to **target** mRNA in)
- IT Diagnosis
 Nucleic acid hybridization
 (nuclease-resistant oligonucleotide **probes** for)
- IT **Functional groups**

Tran 09/738,954

(phosphodiester, of 3'-terminal linkage in oligonucleotide,
modification of, for gene expression inhibition)